Down Memory Lane

Founder Chairman Mr M Manal felicitates Dr Rustom Jal Vakil on his path-breaking work on hypertension published in the *British Heart Journal*.

The product used by Dr Vakil was Serpina (Himalaya).

The first Head of R&D of The Himalaya Drug Company, Dr Roshan M Captain (second from left) with Dr Rustom Jal Vakil (third from left), founder Chairman Mr M Manal (third from right) and other distinguished guests at the felicitation function.
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Message from the Chairman

The Himalaya Drug Company was founded by my father in 1930, long before I was born, with a clear vision to bring Ayurveda to society in a contemporary form. New formulations were created by referring to ancient Ayurvedic texts, selecting widely available Indian herbs and subjecting dozens of these herbs and combinations to modern pharmacological, toxicological, and safety tests to create new drugs and therapies. The most promising formulations then underwent clinical trials by doctors and institutions of modern medicine. The breakthrough came in 1949 (after I was born!) when the British Heart Journal published the work of India’s pioneer in cardiology, Dr Rustom Jal Vakil. He researched Rauwolfia serpentina, the world’s first successful blood pressure lowering agent. The product Dr Vakil used for his work was Serpina (Himalaya)!

As an offshoot of this vision, in the year 1961, The Himalaya Drug Company started publication of the journal “Probe—Exploring ancient and modern medical learning” with the objective to provide latest research updates to the medical community. It was the belief of its publishers that, through high standards of medical journalism and usefulness, Probe would be accepted by doctors all over the nation.

Over the years, the readership of Probe increased in volumes and the publication spread its wings overseas. Today, Probe is read in more than 35 countries.

With great humility, I present to you the 50th anniversary issue of Probe. On this occasion, I thank you, our readers, for your kind support through the years, for your trust and prescriptions of Himalaya products and for being a part of this milestone moment.

Warm personal regards,

Meraj Manal
Chairman
Himalaya Global Holdings Ltd.
(Parent of The Himalaya Drug Company Worldwide)
meraj.manal@himalayaglobalholdings.com
Rauwolfia serpentina (Apocynaceae)
a.k.a. Surpargandha (Sanskrit), Rauwolfia (English).

The pharmacological properties of Rauwolfia serpentina were first discovered by the founder of The Himalaya Drug Company. This led to the introduction of Serpina®, the world’s first antihypertensive drug in 1934.
Editorial

In 1961, The Himalaya Drug Company published the first issue of “Probe—Exploring ancient and modern medical learning” with an objective of providing latest updates to the medical community. We are delighted to bring to you this special issue of Probe on the occasion of completion of 50 golden years of this journal.

In this special issue, we have featured varied series of articles that encapsulates the journey of this journal as well as The Himalaya Drug Company over the past half century. As the editor of Probe, I would like to thank all the authors and editorial assistants for their contribution to this remarkable accomplishment. It almost goes without saying but I should also thank all readers who have collectively made Probe the success that it is.

Please write to us at publications@himalayahealthcare.com with your valuable feedbacks and suggestions on this special issue of Probe.

Dr Pralhad S Patki, MD
Editor in chief
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A B S T R A C T

Aim: The present study was designed to study the genotypes associated with different groups of chronic liver disease and to see their response to HD-03/ES on chronic HBV patients.

Methods: A total of 51 patients with chronic liver disease were recruited in the study and were given HD-03/ES, two capsules twice daily for 6 months. Liver function tests were done every month after initiating treatment. Serum was analyzed for HBsAg, HBeAg, and HBV DNA and quantitative estimation of HBV was done at baseline and 4 and 6 months after therapy. Also, the genotype of all cases was determined using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method.

Results: After 6 months of therapy with HD-03/ES, significant reduction in alanine transaminase (ALT) values from 71.2 ± 16.3 to 36.4 ± 6.8 and significant HBeAg loss (27.4%) and HBV DNA loss (27.4%) were observed. Adverse effects were mild. Genotype D was found in 39 (76.5%) while genotype A was found in 12 (33.5%) cases, respectively. The mean reduction in viral load was observed from log_{10} 7.1 ± 1.8 copies/mL to log_{10} 4.4 ± 1.1 copies/mL. However, a sharp decline in viral load was observed in patients infected with genotype A (log_{10} 6.8 ± 2.5 to log_{10} 4.9 ± 1.8; P<.01) compared to genotype D (log_{10} 7.0 ± 2.6 to log_{10} 5.9 ± 3.5; P = .074).

Conclusion: The study had shown that majority of the patients with chronic HBV-related liver disease had genotype D. In addition, HD-03/ES had a better therapeutic capability of lowering the HBV viral load in patients with genotype A, which needs to be validated in larger studies.

Key Words
HBV, viral load, genotype, chronic liver disease

Introduction
Hepatitis B virus (HBV) infection is a major public health problem, with approximately 350 million individuals chronically infected worldwide. HBV is highly endemic in sub-Saharan Africa, China, and Southeast Asia. It is also highly endemic in the Mediterranean basin and is present at significant levels in most industrialized countries. As compared to Europe and North America, the prevalence of HBV infection in Asia is quite high, with 40 million people harboring chronic HBV infection in India (according to WHO). Although transitional forms exist, chronic HBV infection can be categorized into two forms based on the presence or absence of HBe antigen. Chronic HBV carriers are exposed to a risk of complications such as chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Up to one million people die every year from the complications of HBV infection.

Prevalence of hepatitis B surface antigen (HBsAg) in India varies from 1% to 13%, with an average of 4.7%. High prevalence rates of HBsAg have been noted among the Indian tribal population. Various studies have examined the proportion of persons with HBV infection among persons
with chronic liver disease. Among patients diagnosed with chronic liver disease, the prevalence of HBsAg ranged from 33% to 75%. Other series of patients with cirrhosis show HBsAg positivity ranging from 56% to 70% of cases. Histopathological studies of patients with liver cancer indicate evidence of HBV infection in 60% to 70% of cases.

Ayurveda, an indigenous system of medicine in India, has a long tradition of treating liver disorders with plant drugs. On the basis of the leads available from traditional usage and recent experimental studies, HD-03/ES (a capsule formulation consisting of hydroalcoholic extracts of the herbs *Cyperus rotundus* and *Cyperus scariosus*) was evolved to elicit hepatoprotective activity. Surface antigen suppression and HBV elimination activities of herbal extract containing *C rotundus* and *C scariosus* were examined using two HBsAg expressing human hepatocellular carcinoma cell lines—PLC/PRF/5 and HepG2 2.2.15. Polymerase chain reaction (PCR) for the study of amplification of DNA specific to HBV, reverse transcriptase inhibition assay, immunomodulatory effects, and hepatoprotective ability against oxidative damage to hepatocytes were some of the other studies performed to evaluate the efficacy of the plant extract. An investigation showed that the extracts could reversibly inhibit cell growth and suppress HBsAg expression in both of the human hepatocellular carcinoma cell line models.

Acute and subacute toxicity studies conducted in rats indicated that HD-03/ES is devoid of significant toxicity following acute and repeated administration in rats. However, a preliminary case study report of a patient with chronic hepatitis B showed that there was a significant reduction of HBsAg along with the disappearance of viral DNA following the treatment with HD-03/ES at a dosage of two capsules twice daily for a period of 6 months.

Another recent study also observed a significant HBsAg loss, HBeAg loss, and HBV DNA loss after a period of 6 months therapy with HD-03/ES. However, there is no data available in north Indian patients to show whether HD-03/ES is adequate for the treatment of HBV infection. Therefore, this clinical study was conducted to evaluate the safety and efficacy of HD-03/ES in patients with chronic hepatitis B infection.

**Materials and Methods**

**Patients**

An open-labeled clinical trial was conducted in 51 patients with chronic liver disease to evaluate the safety and efficacy of HD-03/ES capsules alone in the management of chronic hepatitis B infection. The study included 41 (80.4%) patients with chronic hepatitis and 10 (19.6%) patients with decompensated cirrhosis admitted in the medical wards of Lok Nayak hospital and associated Maulana Azad Medical College, New Delhi, between June 2005 and May 2009. Informed written consent was obtained from all participants and the protocol of the study was approved by the ethical committee of the institute. The study in general was conducted in accordance with the Declaration of Helsinki and GCP Guidelines issued by the Ministry of Health, Government of India.

**Diagnostic criteria**

HBV-infected patients showing symptomatic, biochemical (alanine aminotransferase [ALT] more than upper limit of normal), or serological (hepatitis B surface antigen [HBsAg], hepatitis B e antigen [HBeAg], Immunoglobulin G antibodies to hepatitis B core antigen [anti-HBc IgG] positivity) evidence of continued liver disease for >3 to 6 months without steady improvement were diagnosed with chronic hepatitis B (CHB). The diagnosis of cirrhosis was established by clinical history or the presence of ascites and esophageal varices with small, irregular liver surface, altered echotexture, and splenomegaly. Hepatocellular cancer (HCC) was diagnosed on the basis of either pathological or cytological examination or an elevated fetoprotein level (>400 ng/mL) combined with at least one positive image on angiography, sonography, and/or computerized tomography.

**Criteria for enrollment**

Patients, aged between 18 and 60 years, with their serum ALT level of 41 to 200 IU/L and positive serum HBsAg were enrolled to the study.

**Exclusion criteria**

Patients aged >60 years or <18 years; pregnant or lactating women; patients with hepatitis C or other hepatic viral infection, autoimmune hepatitis, and drug-induced or alcoholic hepatitis; patients with severe complications of the cardiovascular, renal, or hematopoietic system; and patients with mental diseases were excluded from the study. Patients with a history of using interferon/ antiviral agents or corticosteroids/ immunosuppressive drugs were also excluded from the study.

**Treatment**

Each patient was asked to take two capsules of HD-03/ES (The Himalaya Drug Company, Bangalore, India) twice daily, two capsules in the morning and two capsules at bedtime after food, for a period of 6 months.
The dosage proposed in this study was based on the dose escalation and safety studies conducted on human volunteers.

Symptoms and signs
Symptoms and signs of patients were recorded in detail using the “Clinical Observation Table” once a month before and during the treatment.

Liver function
Liver function examinations, including contents of serum proteins, total bilirubin (TB), and activities of ALT and aspartate aminotransferase (AST), were done every month during the treatment.

Etiological markers of hepatitis B
Serum samples collected from patients were stored at −20°C until analysis. Serum was assayed for HBsAg, anti-HBc IgG, HBeAg, and HBV DNA at baseline and 4 and 6 months after therapy using commercially available enzyme-linked immunosorbent assay kit.

HBV DNA detection (qualitative) from serum
DNA was extracted using phenol chloroform method.

PCR amplification of HBV DNA
HBV DNA was detected by an inhouse nested PCR technique, amplifying two different regions of the HBV genome.

HBV DNA quantification by real time PCR
Single tube assay with fluorescent hybridization probes and LightCycler Technology was used to determine the HBV viral load. PCR amplification of S gene of HBV for genotyping

Table 1. Demographic Characteristics of Patients at the Baseline

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n = 51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>37.5 ± 7.8</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>38 (74.5%)</td>
</tr>
<tr>
<td>Females</td>
<td>13 (25.5%)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>59.2 ± 6.3</td>
</tr>
</tbody>
</table>

End points
The primary end point was HBsAg clearance. Secondary end points included HBV DNA levels and ALT normalization to 40 IU/L at the end of the treatment.

Statistical analysis
The intention-to-treat analysis included all patients who were HBsAg positive at baseline and received at least one dose of the study medication. Data were expressed as mean ± SD. One-way ANOVA with Bonferroni’s multiple comparison test or Dunnett’s multiple comparison test was performed wherever appropriate using GraphPad Prism version 4.00 for Windows, GraphPad Software, San Diego, CA, USA. A P value of <.05 was considered as statistically significant.

Results
This open study included 51 patients (38 males and 13 females) aged between 19 and 51 years with a mean age of 35.9 years. The baseline characteristics of the study subjects are shown in Table 1.

Clinical response
Six months of therapy with HD-03/ES capsules was significantly effective in the majority of patients as it resulted in disappearance or alleviation of major clinical symptoms such as abdominal pain and poor appetite. The effect of 6 months of treatment with HD-03/ES on liver function tests showed a trend toward
normalization of liver function tests in all patients (Table 2). There was a significant reduction in the levels of ALT from initial value of 71.2 ± 16.3 to 36.4 ± 6.8 (P < .01). In 32 of the 51 patients (62.7%), ALT levels were normalized. Although ALT levels were not normalized in the remaining 19 patients, there was a trend toward reduction and an increase in ALT levels was not observed in any of the patients.

**Virological response**

The effect of 6 months of treatment with HD-03/ES treatment on virological response is shown in Table 3. At the end of treatment, 6 of the 51 patients (11.8%) treated with HD-03/ES had undetectable HBsAg. Also, HBeAg loss 14/51 (27.4%) and HBV DNA loss 14/51 (27.4%) were observed during the treatment with HD-03/ES in patients who were initially positive for both HBeAg and HBV DNA. The mean baseline viral load of the 14 patients who cleared the HBV DNA was log₁₀ 4.8 ± 0.79 copies/mL. Among these 14 patients only 6 patients cleared the virus at the end of 6 months. However, hepatitis B viral load decreased significantly at the end of 6 months and subsequently cleared after 12 months of therapy with HD-03/ES in the remaining 6 patients.

Genotype D was found in 39 (76.5%) while Genotype A was found in 12 (33.5%) patients, respectively. The mean reduction in viral load was observed from log₁₀ 7.1 ± 1.8 to log₁₀ 4.4 ± 2.1 (P < .01). However, a sharp decline in viral load was observed in patients infected with genotype A (log₁₀ 6.8 ± 2.5 to log₁₀ 4.9 ± 1.8; P < .01) compared to genotype D (log₁₀ 7.0 ± 2.6 to log₁₀ 5.9 ± 3.5; P = .074) (Figure 1).

**Adverse events**

HD-03/ES was well tolerated in this study. No patient was withdrawn from therapy either for adverse effects or for other reasons. Most of the observed side effects (such as fatigue, headache, and insomnia) were mild in nature. The most common adverse event was abdominal discomfort. No serious biochemical abnormalities were experienced by any patient.

### Table 2. Response of HD-03/ES on the Liver Function Profile of the Subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>4th month</th>
<th>6th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (IU/L)</td>
<td>51.6 ± 7.8</td>
<td>45.6 ± 5.9</td>
<td>42.3 ± 8.1</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>71.2 ± 16.3</td>
<td>46.2 ± 7.9</td>
<td>36.4 ± 6.8</td>
</tr>
<tr>
<td>Serum bilirubin (mg%)</td>
<td>1.3 ± 0.8</td>
<td>1.2 ± 0.6</td>
<td>1.1 ± 0.5</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU/L)</td>
<td>159.7 ± 13.8</td>
<td>145.2 ± 10.6</td>
<td>131.1 ± 8.7</td>
</tr>
<tr>
<td>Total protein (g%)</td>
<td>6.3 ± 0.8</td>
<td>6.5 ± 0.9</td>
<td>6.6 ± 0.4</td>
</tr>
<tr>
<td>Serum albumin (g%)</td>
<td>3.5 ± 0.7</td>
<td>3.5 ± 0.5</td>
<td>3.6 ± 1.2</td>
</tr>
<tr>
<td>Serum globulin (g%)</td>
<td>2.9 ± 0.5</td>
<td>3.1 ± 0.4</td>
<td>3.2 ± 0.7</td>
</tr>
</tbody>
</table>

### Table 3. Presentation of Viral Factors at Baseline and After 6 Months of Therapy

<table>
<thead>
<tr>
<th>Viral factors</th>
<th>Baseline</th>
<th>4th month</th>
<th>6th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>51</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBeAg</td>
<td>51</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBV DNA</td>
<td>51</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean viral load log₁₀ (copies/mL)</td>
<td>71 ± 1.8</td>
<td>6.6 ± 0.8</td>
<td>4.4 ± 1.1</td>
</tr>
</tbody>
</table>

**Discussion**

High morbidity and mortality among HBsAg-positive patients, even in the absence of overt liver disease, have been found in Asia. The goals of treatment in CHB infection are sustained viral suppression, normalization of ALT levels, and improvement in liver histology leading to long-term reduction in the risk of cirrhosis and hepatocellular carcinoma. Loss of HBsAg and HBeAg and normalization of ALT levels and improvement in liver histology are the usual short-term end points of therapy. Results of this study indicated that short-term therapy with HD-03/ES is effective in the management of CHB. The initial results of this study are promising, and hence the therapy was extended in six responders that showed complete viral clearance including HBsAg, HBeAg, and HBV DNA viral copies.

The ultimate end point of antiviral therapy for CHB infection is the loss of HBsAg, which is accompanied by disease remission in terms of ALT normalization. In this study, HBsAg loss was observed in 11.8% of the patients after 6 months of therapy with HD-03/ES. This is in contrast to several clinical trials of antivirals where HBsAg loss was not reported or tends to occur later than 24 weeks as with interferon therapy. Although 6 months of therapy is limited and not capable of inducing pronounced viral suppression, HBV DNA loss was observed in 6 patients following 6 months of therapy, which is highly encouraging.

HBeAg loss, either spontaneously or following therapy, significantly improves the clinical outcome and survival in chronic HBV patients. Therefore, HBeAg loss has remained as a major end point of antiviral
therapy in chronic HBV infection. Monotherapy with α-interferon for 16 to 26 weeks is associated with the loss of serum HBeAg in 20% to 40% of the patients. Results (27%) of the present study are comparable to the interferon therapy. HD-03/ES also plays an important role in lowering the viral load in almost all of the patients in this study. Further, a sharp decline in viral load was observed in patients infected with genotype A compared to genotype D.

The possible mechanisms of action as studied using HBsAg expressing human hepatocellular carcinoma cell lines PLC/PRF/5 and HepG2 2.2.15 indicate HBsAg suppression by binding to the antigen, and HBV elimination by reverse transcriptase inhibition. Immunomodulatory effects occur by causing the release of nitric oxide (NO) by macrophages and cytokines like TNF-α. It was found to have a hepatoprotective effect by reversing the oxidative damage caused by hepatocytes. A strong correlation was found between HBV DNA levels and histology activity index scores in HBeAg negative patients. In the present study, findings such as ALT normalization, HBeAg loss, and loss of DNA during short-term treatment with HD-03/ES indicated that patients treated with HD-03/ES may lose their infectivity faster and relapse rates would be low.

Conclusion
This trial demonstrated that 24 weeks of HD-03/ES treatment resulted in clinically significant virological and biochemical benefits in patients with CHB infection. Further, 6 months extended therapy conferred comparatively better results in terms of viral clearance. Therefore, it can be concluded that HD-03/ES is beneficial in the management of CHB.

Common Signs of Aging Traced to Tiny Brain Blockages

Blocked blood vessels in brain, often too small to be seen with medical imaging technologies, may explain some of the common signs of aging such as diminished walking ability and hand tremors. Brain autopsy findings showed microscopic infarcts in 57 individuals out of 418 examined, the presence of which was significantly associated with gait abnormalities similar to those seen in Parkinson disease, according to Aron S Buchman, MD, Rush University in Chicago, and colleagues. Signs of arteriolosclerosis invisible with standard imaging were also significantly associated with Parkinsonian gait, as were macroscopic infarcts that would be picked up with computerized tomography or magnetic resonance imaging scans, the researchers indicated online in Stroke, a journal of the American Heart Association.

Evaluation of Efficacy and Safety of a Herbal Formulation Cystone in the Management of Urolithiasis: Meta-analysis of 50 Clinical Studies

Karamakar D, et al.

**ABSTRACT**

The aim of this study was to carry out the meta-analysis of 50 clinical trials to evaluate the efficacy and safety of Cystone in urolithiasis. Total 50 clinical studies conducted at various centers between 1954 and 2004 have been taken into account, which comprised 3037 patients (Cystone: 1837 and others: 1200 of either sex). The demographic data of patients on entry was tabulated from each study. The duration of treatment varied from 2 weeks to 2 years and in most of the studies, except in pediatric patients, Cystone was used at a dosage of 2 tablets thrice daily. Parameters such as size of renal calculi, clearance of calculi with reference to location of calculi, symptomatic relief, and urinary excretion of stone-forming constituents were evaluated. Results of this study indicated a significant symptomatic relief in Cystone group. Cystone treatment resulted in a significant reduction in 24-hour urinary excretion of oxalate \( P < .01 \), uric acid \( P < .01 \), calcium \( P < .01 \), magnesium, and phosphorus with a significant increase in urine volume \( P < .01 \). This analysis also indicated the safety profile of Cystone. There have been no reports of any serious adverse effects or mortality due to Cystone treatment. The outcome of 50 clinical studies showed that Cystone is useful in the management of urolithiasis as indicated by the clearance of calculi, symptomatic relief, increased urine volume, and reduction in the stone-forming constituents in urine.

**Key Words**
Meta-analysis, urolithiasis, hypercalciuria, hyperoxaluria, cystinuria

**Introduction**

Urolithiasis or renal calculi are crystal aggregations of dissolved materials in the urine and hence the process is called urolithiasis. The sequence of formation of urinary stone involves urinary saturation, urinary supersaturation, nucleation, crystal growth, crystal aggregation, and urinary stone formation. Urinary stones are formed because of metabolic disturbances such as hypercalciuria, hyperoxaluria, and cystinuria. Sometimes, urinary stones are formed because of chronic urinary tract infections (UTIs). Urinary stones can be of calcium, cystine, uric acid, or struvite stones. They typically form inside the kidney (nephrolithiasis), ureter (urolithiasis), or urinary bladder. These calculi can vary in size and shape and when they grow up to 2.3 mm, they can cause obstruction of the ureter. This may lead to obstruction with dilation or stretching of the upper ureter and renal pelvis as well as spasm leading to severe episodic abdominal pain, which may be associated with nausea and vomiting. At present, no medical therapy is available for dissolution or displacement of renal stones. A number of herbs and their combinations have been claimed to have beneficial effects in urolithiasis. Cystone is a herbomineral formulation specifically developed for the
management of urolithiasis or renal calculi. This formulation is being used extensively in the management of urolithiasis. Till date, 80 clinical trials have been carried out to evaluate the safety and efficacy of Cystone in the management of urolithiasis. The present study was conducted to review the meta-analysis of 50 of these clinical trials, so as to arrive at the status of Cystone in the management of urolithiasis.

**Aim of the Study**

The aim of this study was to carry out the meta-analysis of 50 clinical trials for identifying the efficacy and safety of Cystone in urolithiasis.

**Material and Methods**

**Study design**

This is a cumulative meta-analysis of 50 published clinical trials of Cystone in urolithiasis.

**Study period**

This study evaluated the clinical trials of Cystone conducted between 1954 and 2004.

**Inclusion criteria**

All published studies, which evaluated the role of Cystone in urolithiasis, were included in the meta-analysis irrespective of the study design. The meta-analysis included clinical trials, which were either controlled studies or open clinical studies. There were no restrictions regarding sex, age, or duration of disease. The outcome variables included measurement data on changes in clinical symptoms and signs, laboratory results, and incidence of adverse events during/after treatment.

**Exclusion criteria**

Experimental, Phase I, and Phase II studies were excluded from the study population.

**Study procedure**

In all, 50 clinical studies done at various centers between 1954 and 2004 were taken into account. From each study, the demographic data of patients on entry was tabulated. The duration of treatment varied from 2 weeks to 2 years (Table 1) and in most of the studies, except in pediatric patients, Cystone was used at a dosage of 2 tablets thrice daily. Changes in the clinical and biochemical parameters were taken into account in addition to the calculi size, location of the calculi, urine volume and urinary excretion of oxalate, uric acid, and calcium. Studies that considered parameters like burning micturition, bacturia, and the presence or absence of pus cells in the urine of urolithiasis patients, were also taken into account. The predefined primary end points in majority of these studies have been clearance of renal calculi and relief from clinical symptoms.

**Adverse events**

The incidence and type of adverse events reported by various studies were also tabulated separately. All adverse events, either reported or observed by patients, were recorded with information about severity, duration, and action taken regarding the study drug. Relation of adverse events to study medication was predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence from the administration of the drug), “Possible” (follows a known response pattern to the suspected drug, but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state).

**Statistical analysis**

Statistical analysis was done according to intention-to-treat principles. Changes in various parameters from baseline values and values at the end of the study were pooled and analyzed cumulatively using Fisher’s Exact Test, Paired t-test, or repeated measures of ANOVA, followed by Dunnett’s multiple comparison test. Values are expressed as mean ± SD or as incidences of patients with or without symptoms. The minimum level of significance was fixed at 95% confidence limit and a two-sided P value of <.05 was considered significant. Statistical analysis was performed using GraphPad Prism software (Version 4.01).

**Results**

In all, the study included 50 clinical trials, which involved 3037 patients (Cystone: 1837, Others: 1200) of either sex. The age range of patients included in all studies was 1 to 72 years and the duration of treatment is 2 weeks to 2 years (Table 1).

In 636 patients, data were available regarding the calculi size and analysis of this data indicated that there was a significant decrease in presence of renal calculi (Table 2) and the calculi size decreased from 6.21 ± 4.24 mm to 0.57 ± 0.79 mm (P<.0067).

In one of the studies, antispasmodic medications, forced diuresis, and

<table>
<thead>
<tr>
<th>Table 1. Demographic Data with Dose and Duration of Cystone Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic data</td>
</tr>
<tr>
<td>Number of trials</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Age of patients</td>
</tr>
<tr>
<td>Dose</td>
</tr>
<tr>
<td>Duration of treatment</td>
</tr>
<tr>
<td>*In case of pediatric patients, ½ to 1 tablet TID.</td>
</tr>
</tbody>
</table>
Clinical insight

Table 2. Effect of Cystone on Clearance of Renal Calculi and Calculi Size

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cystone</th>
<th>Other treatment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of renal calculi</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td></td>
<td>636</td>
<td>78 (87.73%)</td>
</tr>
<tr>
<td></td>
<td>(P &lt; .0001)</td>
<td></td>
</tr>
<tr>
<td>Calculi size (mm) (n = 339)</td>
<td>6.21 ± 4.24</td>
<td>0.57 ± 0.79</td>
</tr>
<tr>
<td></td>
<td>(P &lt; .0007)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not available</td>
<td></td>
</tr>
</tbody>
</table>

*Antispasmodics (tablets in mild cases and parenteral injections in cases of severe colic), forced diuresis, and IV fluids.

Statistical analysis: Fisher’s exact test for presence of renal calculi and Paired t test for calculi size.

Table 3. Effect of Cystone on Clearance of Calculi Based on its Location

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of trials</th>
<th>No. of patients</th>
<th>Age (years)</th>
<th>Dose</th>
<th>Duration of treatment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal</td>
<td>21</td>
<td>71</td>
<td>1–72</td>
<td>2 TID</td>
<td>2 weeks to 6 months</td>
<td>52 (73.24%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 TID</td>
<td></td>
<td>19 (26.76%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(P)</td>
<td></td>
<td>(P &lt; .0001)</td>
</tr>
<tr>
<td>Ureteric</td>
<td>36</td>
<td>528</td>
<td>1–72</td>
<td>2 TID</td>
<td>2 weeks to 6 months</td>
<td>475 (89.96%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 TID</td>
<td></td>
<td>53 (10.04%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(P)</td>
<td></td>
<td>(P &lt; .0001)</td>
</tr>
<tr>
<td>Bladder/vesicle</td>
<td>15</td>
<td>37</td>
<td>1–60</td>
<td>2 TID</td>
<td>2 weeks to 6 months</td>
<td>31 (83.78%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 (16.22%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(P &lt; .0001)</td>
</tr>
</tbody>
</table>

Note: P—Pediatric patients.
Percent response is shown in parentheses.

Table 4. Effect of Cystone and Other Treatments on Burning Micturition, Bacteriuria, and Pus Cells

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cystone</th>
<th>Other treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Burning micturition</td>
<td>Before</td>
<td>433</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteriuria</td>
<td>Before</td>
<td>276</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pus cells</td>
<td>Before</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dose: Cystone 2 tablets TID for 1 to 6 months. Other treatment: Burning micturition: Patients were given urinary antiseptics such as nitrofurantoin, ampicillin, cotrimoxazole, sulfonamides, or chloramphenicol alone. Bacteriuria: Ampicillin 250 mg, 6 hourly for 7 days, Alkaline mixture and cotrimoxazole BID for 5 days. Pus cells: Conventional therapy for UTI or antibiotics prescribed based on culture sensitivity reports. Statistical analysis: Fisher’s exact test.

Table 5. Adverse drug reactions

<table>
<thead>
<tr>
<th>Adverse effects</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspepsia</td>
<td>3</td>
</tr>
<tr>
<td>Flatulence</td>
<td>4</td>
</tr>
<tr>
<td>Gastric irritation</td>
<td>3</td>
</tr>
</tbody>
</table>

IV fluids were used in 50 patients, which showed significant decrease in presence of renal calculi (Table 2).

The effect of Cystone on clearance of calculi based on its location is shown in Table 3. It was observed that although effective in renal, ureteric and vesical calculi, Cystone showed better results in ureteric calculi as compared to other sites. The clinical response in ureteric calculi was 89.96%, whereas in renal calculi it was 73%. The results also indicated that in renal calculi, 27% of the patients required interventional surgery as compared to only 10% of patients in case of ureteric calculi (Table 3).

The meta-analysis also indicated that Cystone improved urinary volume to a significant level in a period of 8 weeks (Figure 1). Also, it significantly decreased oxaluria, uric acid, and calcium in the urine (Figures 2 and 3).

The analysis also indicated that Cystone resulted in significant symptomatic relief, as compared to other treatment groups, in burning micturition and reduces bacteriuria and pus cells in patients with UTI (Table 4).

Adverse effects

The adverse effects reported in these studies have been dyspepsia, flatulence, and gastric irritation (Table 5). However, none of the patients had to withdraw from the Cystone therapy because of adverse effects. In addition, there were no reports of any serious adverse effects or mortality due to Cystone therapy.

Discussion

Cystone is a herbomineral formulation designed and developed for the management of urolithiasis or renal calculi. This product came into
existence in 1943, and since then this product has been in use all over the world for the management of urolithiasis and UTI. In studies conducted till date, Cystone has proven to be significantly effective (80%) in patients with urolithiasis.

In the present study, clinical trials and their details were tabulated and analyzed statistically. In case of all or none phenomenon (resolved and unresolved), Fisher’s exact test was utilized. In case of within the group comparison (before and after drug therapy in the same patients), Student’s t test was employed. In case of comparison between different intervals, repeated measures of ANOVA test was employed for meta-analysis.

Various studies of Cystone in urolithiasis can be broadly categorized into controlled and uncontrolled studies. The number of uncontrolled studies was more as compared to controlled studies, especially the studies conducted before 1995. Nonrandomized studies (controlled, uncontrolled, case reports, and cross-sectional surveys) confirmed the findings of a systematic review of randomized trials. They also provide information on long-term effects, prognostic factors, and adverse effects. While these may not be conclusive, they can provide useful summaries of the state of knowledge. However, efforts were made to document the efficacy of Cystone by averaging different clinical trials. Even in controlled studies, comparisons were made with respect to different modalities like forced diuresis, antispasmodics, etc. The number of uncontrolled (open trial) and controlled trials of Cystone in urolithiasis was 23 and 8, in burning micturition it was 2 and 1, and in bacteuria/pus cells it was
6 and 5, respectively. The placebo-controlled clinical trials were very few. Nevertheless, an overview of these clinical trials indicated that Cystone is efficacious in the management of urolithiasis, especially when the site of urinary stone is ureter. The results obtained in urolithiasis were better as compared to nephrolithiasis. Few of the studies evaluated the efficacy of Cystone in pediatric population and stone formers. A double-blind placebo controlled study on pediatric urolithiasis involved 87 patients and the duration of treatment was 4 months. This study indicated significant symptomatic relief in patients of Cystone group along with significant reduction in 24-hour urinary excretion of calcium, magnesium, and phosphorus.

This analysis also indicated safety profile of Cystone. The adverse effects have been dyspepsia, flatulence, and gastric irritation, which did not necessitate withdrawal of the drug. None of the studies were aimed to describe the mechanism of activity of Cystone.

In spite of large number of clinical trials conducted, a number of lacunae (few controlled trials and lack of dose dependent studies) still exist. These studies if carried out will go a long way in defining the role of Cystone in the management of urolithiasis.

Conclusion

The outcome of 50 clinical studies indicated that Cystone is useful in the management of urolithiasis as revealed by the clearance of calculi, symptomatic relief, increased urine volume, and reduction in the stone forming constituents in urine with negligible adverse effects.

Osteoporosis Screening and Treatment Guidelines: Are They Being Followed?

This study was conducted to examine a cohort of women sent for dual-energy x-ray absorptiometry (DXA) screening to see whether they met the criteria for bone density testing. In addition, the researchers sought to determine whether they were receiving appropriate interventions based on published guidelines.

Between January 1, 2007 and March 1, 2009, inclusive, postmenopausal women (age >49 years) sent for DXA bone density screening were offered enrollment into the study. Risk factors for osteoporosis, demographic information, and current DXA results were recorded. The 2006 Osteoporosis Position Statement of The North American Menopause Society was used for screening and therapeutic intervention guidelines.

Among the 615 women with data, the mean (SD) age was 61.5 (8.3) years. Using the 2006 guidelines of The North American Menopause Society, 41.3% (253 of 612) of the women who had DXA testing did not meet the criteria for such screening. Of these women, 25.5% (157 of 615) were not taking calcium, 31.1% (191 of 614) were not taking vitamin D, and 59.8% (343 of 574) were not exercising at least half an hour per week. Of the women with any of the approved indications for treatment, 15.7% (16 of 102) were not taking calcium, 18.6% (19 of 102) were not taking vitamin D, 52.7% (49 of 93) were not exercising at least 2 hours per week, and 35.3% (36 of 102) were not receiving therapy. In contrast, of those women without an indication for treatment, 17.8% (83 of 467) were receiving bisphosphonate, raloxifene, or calcitonin therapy.

A large number of women are not properly screened or treated for osteoporosis. Inappropriate screening may also lead to improper management of osteoporosis and its associated complications.

What Every Gastroenterologist Needs to Know About Common Anorectal Disorders

Schubert MC, et al.


**Introduction**

Anorectal complaints are very common and are mostly caused by benign anorectal disorders. Although many anorectal conditions may be successfully treated by primary care physicians in the outpatient setting, but patients tend not to seek medical attention due to embarrassment or fear of cancer. As a result, patients frequently present with advanced disease after experiencing significant decreases in quality of life. A number of patients with anorectal complaints are referred to gastroenterologists. However, gastroenterologists’ knowledge and experience in approaching these conditions may not be sufficient. This article can serve as a guide to gastroenterologists in recognizing, evaluating, and managing common benign anorectal disorders, as well as identifying when surgical referrals are most prudent.

**Hemorrhoids**

The estimated prevalence rate of symptomatic hemorrhoids in the United States is 4.4% of the adult population; more than 1 million individuals are affected by hemorrhoidal conditions, annually. Hemorrhoids are cushions of nonpathologic vascular tissue in the anal canal, which microscopically are sinusoids because they do not have any muscle as veins do. Hemorrhoidal tissue is thought to contribute to anal continence because 15% to 20% of resting anal pressure derives from these cushions. The symptoms of hemorrhoidal disease are caused by pathologic and dilated changes in hemorrhoidal tissue.
Clinical insight

Etiology

Proposed etiologic factors include vascular congestion and mucosal prolapse. Vascular congestion could derive from prolonged straining or increased intra-abdominal pressure due to ascites, obesity, or pregnancy. Mucosal prolapse may develop secondary to derangement of the internal sphincter or through aging causing the anatomic structures supporting the muscularis submucosa to weaken, leading to prolapse of the hemorrhoidal tissue. Multiple studies have shown elevated anal resting pressure in patients with hemorrhoids.

Symptoms

Patients often self-refer with symptoms of itching, pain, or bleeding per the rectum. To the general population, anything problematic around the anus is suspected to be hemorrhoids. Internal hemorrhoids may prolapse or bleed, but rarely become painful unless they develop thrombosis or necrosis. Thus, anal pain usually suggests other pathology and mandates closer investigation. About 20% of patients with hemorrhoids have concomitant anal fissure(s). Usually, painless bright red bleeding that stains the water in the toilet occurs from internal hemorrhoids. This bleeding is arterial, from presinusoidal arterioles, and is mostly associated with bowel movements where the stool itself is brown. If rectal bleeding is not typical for hemorrhoidal bleeding as described, a prompt and thorough medical evaluation is warranted. Thrombosed external hemorrhoids may cause significant pain because the anoderm is richly innervated which is exactly why external hemorrhoids should not be ligated or excised without adequate local anesthetics. Skin tags are often confused with symptomatic hemorrhoids. A skin tag is redundant fibrotic skin at the anal verge, often persisting as the residual of a thrombosed external hemorrhoid. It is important to note that there is no increased risk of cancer in hemorrhoids.

Classification

Hemorrhoidal conditions are classified according to their location. External hemorrhoids are situated distal to the dentate line and are covered by anoderm that is sensitive to touch, temperature, and stretch because of innervation by somatic nerves. The dentate line is the junction of ectoderm and endoderm, and therefore represents an important mark between two distinct origins of venous and lymphatic drainage, nerve supply, and epithelial lining. Internal hemorrhoids are covered by columnar or transitional epithelium, located proximal to the dentate line, and are graded based on the degree of the prolapse. First-degree hemorrhoids may bleed and bulge into the anal canal and may prolapse beyond the dentate line on straining. Second-degree hemorrhoids prolapse through the anus but spontaneously reduce. Third-degree hemorrhoids prolapse through the anal canal and require manual reduction. Fourth-degree hemorrhoids prolapse, but are irreducible, and thus are at risk for strangulation. However, most hemorrhoids are a combined type of internal and external hemorrhoids. Prognosis and treatment are mostly based on the classification.

Diagnosis

Patients who complain of hemorrhoids need a careful evaluation to exclude other conditions. Either the prone or the left lateral decubitus position can be used to evaluate the anal area, although the lateral position is easier for pregnant patients and those patients with severe chronic obstructive pulmonary disease. Digital, anoscopy, and sigmoidoscopic examination are important initial evaluations. A thorough examination of the anorectal area is required. Inspection is performed by gentle retraction of the buttocks. The color or condition of the skin should be examined for findings such as swelling, induration, fissure, draining sinuses, or mass. The sacrococcygeal region and the perianal skin should be examined. An anoscopy is done to visualize internal hemorrhoids, which bulge into the lumen of the anoscope when the patient strains. A full examination of the colon with a barium enema or colonoscopy is considered if there are no compatible findings of hemorrhoidal disease, especially in patients older than 40 years.

Treatment

As hemorrhoids are a normal part of anorectal anatomy, treatment is indicated only if they become symptomatic. However, in the general management of hemorrhoids, colorectal surgeons agree that all painful thrombosed hemorrhoids should be excised. Excision is not mandatory in these cases, especially in the absence of erosion or significant tenderness to touch. Initial medical management is recommended for all but the most advanced cases. As a conservative treatment, the universal recommendations are to add dietary fiber, avoid straining during defecation, and to utilize sitz baths two to four times a day. Patients should be educated to increase the intake of water along with dietary fiber.

Hemorrhoids that fail to respond to medical management may be treated with rubber band ligation, sclerosis, and thermotherapy by using infrared...
beam, electric current, CO₂ laser, or ultrasonic energy. These techniques induce scarring and fixation of the hemorrhoids to the underlying tissues. Infrared photocoagulation works well on small bleeding hemorrhoids, but is less effective on large or bulky hemorrhoids. Rubber band ligation has been demonstrated to be the most effective method to treat symptomatic internal hemorrhoids that have failed to respond to conservative management. Complications associated with this procedure are not frequent (<2%) and include vasovagal response, anal pain, bleeding from early dislodgment, and pelvic sepsis. Operative hemorrhoidectomy is reserved for the large third- and fourth-degree hemorrhoids, mixed hemorrhoids with a prominent external component, and incarcerated internal hemorrhoids requiring urgent intervention.

Several randomized trials have compared different types of hemorrhoidectomies with a variety of open and closed techniques with inconsistent results. Similarly, a variety of techniques have been introduced to reduce postoperative pain. The stapled hemorrhoidopexy, also called Procedure for Prolapse and Hemorrhoids (PPH), is a technique that reduces the prolapse of hemorrhoidal tissue by using an intraluminal circular stapling device to remove a ring of redundant mucosa and submucosa from the upper anal canal, thereby reducing the prolapsing hemorrhoidal tissue back into the anal canal and fixing it into position. Compared to conventional hemorrhoidectomy, PPH affects few nerve endings, which results in less post-operative pain. The ultrasonic scalpel hemorrhoidectomy and the bipolar sealing and cutting device have also been reported to produce less postoperative pain than conventional excisional hemorrhoidectomy. However, long-term efficacy needs to be determined.

**Anal Fissures**

An anal fissure is a cut or split in the epithelial lining of the anal canal distal to the dentate line. A chronic anal fissure is usually categorized when the fissure fails to heal within 6 to 8 weeks. Chronic fissures develop ulceration and heaped-up edges with exposure of the internal anal sphincter fiber at the base of the ulcer. There is often an associated external skin tag and/or an internal hypertrophied anal papilla. The vast majority of anal fissures occur in the posterior midline, while 10% to 15% occur in the anterior midline and less than 1% of fissures occur in lateral positions.

**Differential diagnosis**

If an anal fissure develops in atypical locations, one must consider other diseases. Crohn’s disease is the most common cause of anal fissures associated with atypical locations, although other inflammatory bowel diseases, syphilis, tuberculosis, leukemia, cancer, and human immunodeficiency virus (HIV) are also known causes.

**Symptoms**

Anal fissures are the most common causes of severe anorectal pain. Characteristic symptoms include tearing pain with defecation and hematochezia that is usually present as blood on the toilet paper. Patients may also complain of a sensation of intensely painful anal spasms lasting for several hours after a bowel movement.

**Diagnosis**

Anal fissures can be diagnosed through history and physical examination. Gentle spreading of the buttocks to expose the perianal area may facilitate the examination. The fissure is easily visible in the anal canal.

**Pathophysiology**

Although the etiology of this condition is uncertain, the main hypothesis is that the posterior midline area may have decreased blood flow due to the configuration of the vessels of the anus. Also, spasm of the internal anal sphincter may cause further reduction in blood flow.
to the posterior anal canal. Trauma from such factors as hard stools can aggravate the condition, and then eventually cause fissures.

**Treatment**

Medical therapy leads to healing vast majority of patients with acute anal fissures and almost half of the patients with chronic fissures. Therapy focuses on breaking the cycle of pain, spasm, and ischemia thought responsible for the development of the fissure. Initial conservative measures consist of three components: relaxation of the internal sphincter; institution and maintenance of atraumatic passage of stool; and pain relief. These goals can be accomplished with bulk agents and stool softeners, and warm sitz baths following bowel movements to relax the sphincter. On the basis of the theory that anal fissures are caused by ischemia through a spasmodic internal sphincter, pharmacological agents may be useful. These agents have been employed to reduce the resting anal canal pressure and to improve blood flow, and as an alternative to surgical sphincterotomy for chronic fissures. Despite relatively good efficacy, medical therapy has some limitations with poor compliance, unpleasant side effects, and recurrence of fissures. Surgical treatment is generally reserved for fissures that have failed medical therapy. A recent meta-analysis of four randomized, controlled trials revealed superior fissure healing rates with lateral internal sphincterotomy compared with topical nitroglycerin. Lateral internal sphincterotomy is the procedure of choice for the majority of surgeons.

**Anal Fistulas and Anal Abscesses**

An anal fistula is an abnormal connection between two epithelial-lined spaces of the anus and rectum, creating the appearance of a pipe or tube. Anal abscesses and fistulas are the acute and chronic manifestations of the same perirectal pathogenic process. The majority of these conditions originate from infected anal glands.

**Symptoms**

The patient may complain of drainage, bleeding, pain with defecation or sexual activity, swelling, or diarrhea. Fistulas may be related to other diseases such as Crohn’s disease, proctitis, or anorectal cancer.

**Diagnosis**

Physical examination may reveal the external opening as a protrusion or an induration, which drains pus. The risk of incomplete healing, a recurrent fistula, or even inadvertent sphincter injury is increased, if fistula anatomy is incorrectly delineated or an occult abscess is missed. Several imaging modalities are available to evaluate perianal fistulas and abscesses. External lesions seen anterior to this line run directly from the anal canal. If the external opening is detected posterior to this line, the fistula is more complex and tracks laterally around the anus prior to a midline posterior opening. Endoscopy may detect the internal opening. Other methods include passing a probe; injection of a dye such as hydrogen peroxide ($\text{H}_2\text{O}_2$), milk, or methylene blue; fistulography; anal ultrasound with $\text{H}_2\text{O}_2$ injection; and magnetic resonance imaging (MRI). Several studies have concluded that MRI and anorectal endosonography (EUS) are accurate means of delineating anatomy in relation to a fistula.

**Management**

The principal management is surgery. Anal abscesses should always be drained in a timely manner. Delayed or inadequate treatment may occasionally cause extensive or life-threatening suppuration with massive tissue necrosis and septicemia. Thus, an early referral to a specialist is recommended. The goals of surgical therapy are to remove the fistula tract while preserving fecal continence. The surgical approach depends upon the type of fistula. Simple intersphincteric fistulas can be treated by fistulotomy (opening of the fistula tract). High transspincteric and supraphincteric fistulas are more safely treated by initial placement of a seton.

**Conclusion**

Although most anorectal conditions are benign, knowledgeable and skilled physician intervention is often required. Understanding the pathophysiology of anorectal disease guides treatment selection. Initiating early appropriate treatments should lead to prompt symptomatic resolution in a cost-effective manner. A subgroup of patients who persistently present with symptoms despite applicable conservative or nonsurgical management should be referred to a colorectal surgeon.
Lack of Awareness in Men with Risk Factors for Erectile Dysfunction

Shabsigh R, et al.


### Introduction

Erectile dysfunction (ED) affects quality of life and may be associated with depression. Men with ED often have other comorbidities such as diabetes, hypertension, and coronary artery disease. Conversely, men consulting with their physician for comorbidities or other risk factors for ED may also have underlying ED, which may or may not be recognized. ED is defined as the inability to attain or maintain an erection sufficient for satisfactory sexual performance. However, men who experience a change in their ability to achieve an erection might not immediately recognize that ED is the problem. The quality of men’s erections deteriorates gradually over time. Consequently, men may be uncertain whether their erectile difficulties are permanent or temporary and may wait to see if the ED resolves on its own. Alternatively, the stigma or embarrassment of having ED symptoms may lead to denial of the problem.

The authors hypothesized that men with comorbidities and risk factors associated with ED frequently have this condition but might deny it and not identify themselves as ED sufferers. The current report discusses the design and outcome of a screening strategy for men with ED-associated comorbidities and risk factors who do not self-identify as having ED.

### Abstract

Men with erectile dysfunction (ED) often have concurrent medical conditions. Conversely, men with these conditions may also have underlying ED. The prevalence of unrecognized ED in men with comorbidities commonly associated with ED was determined in men invited to participate in a double-blind, randomized, placebo-controlled trial of sildenafil citrate.

Men, aged ≥30 years, presenting with ≥1 ED risk factor (controlled hypertension, hypercholesterolemia, smoking, metabolic syndrome, stable coronary artery disease, diabetes, depression, lower urinary tract symptoms, obesity [body mass index ≥30 kg/m²], or waist circumference ≥40 inches), and not previously diagnosed with ED were evaluated. The screening question, “Do you have erectile dysfunction?,” with responses of “no,” “yes,” and “unsure,” and the Erectile Function domain of the International Index of Erectile Function (IIEF-EF) were administered.

Of the 1084 men screened, 1053 answered the screening question and had positive IIEF-EF scores. IIEF-EF scores indicated ED in 71% (744/1053) of men, of whom 54% (399/744) had moderate or severe ED. Some degree of ED was observed in 96% of men answering “yes,” 90% of men answering “unsure,” and 36% of men answering “no.” The mean ± SD (range) of risk factors was 2.9 ± 1.7 (3–8) in the “yes” group, 3.2 ± 1.7 (3–9) in the “unsure” group, and 2.6 ± 1.5 (2–8) in the “no” group.

Although awareness of having ED was low, most men with risk factors had IIEF-EF scores indicating ED. ED should be suspected and assessed in men with risk factors, regardless of their apparent level of awareness of the condition.

**Key Words**

Erectile dysfunction, risk factors, IIEF-EF scores
The objective was to create a profile of these men by describing the general characteristics (demographics, comorbidities, and risk factors) of men who answered the question, “Do you have erectile dysfunction?” with “yes,” “no,” or “unsure” responses. Such information is needed in order to allow formulation of strategies to identify previously unrecognized or undiagnosed ED in order that it may be addressed as a medical condition.

**Methods**

Men were recruited for a men’s health study without mention of ED. At the screening visit for this sildenafil flexible-dose, double-blind, placebo-controlled trial, written informed consent was obtained, and demographic data and the patient’s history of risk factor(s) were collected. The protocol was approved by the Institutional Review Board of each participating center, and the study was conducted in compliance with ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. Men, aged ≥40 years, who presented with at least 1 risk factor or comorbidity for ED (controlled hypertension, hypercholesterolemia, smoking, metabolic syndrome, stable coronary artery disease, diabetes, depression, lower urinary tract symptoms [LUTS], obesity [body mass index ≥30 kg/m²], or waist circumference ≥40 inches) and who had not been previously diagnosed with ED were eligible for screening. Key exclusion criteria included hypotension, current or anticipated nitrate or nitric oxide donor treatment, significant cardiovascular disease within the past 3 months, and previous use of more than 6 doses of any phosphodiesterase type 5 inhibitor.

Men were asked the screening question, “Do you have erectile dysfunction?” and administered the Erectile Function domain of the International Index of Erectile Function (IIEF-EF). Those who answered “no” or “unsure” to the ED question and who had any degree of ED (scored ≤25 out of 30 on the IIEF-EF) were eligible for inclusion into the double-blind, placebo-controlled trial. The results of the screening analysis are reported here.

**Results**

Of the 1084 men screened, 1079 responded to the ED screening question and 1053 had positive IIEF-EF scores. Overall, IIEF-EF indicative of ED were noted in 71% (744/1053) of men, of whom 54% (399/744) had moderate or severe (IIEF-EF score ≤16), 23% (171/744) had mild-to-moderate (IIEF-EF score 17–21), and 23% (174/744) had mild ED (IIEF-EF score 22–25).

One hundred thirty-nine men responded “yes” to the ED screening question and also completed the IIEF-EF; of these, 96% had IIEF-EF scores consistent with some degree of ED. Among those who answered “no” to the screening question (388/1053), 36% also had IIEF-EF scores that indicated some degree of ED. Among those who answered “unsure” to the screening question (526/1053), 90% had IIEF-EF scores that indicated some degree of ED.

Although the mean age of the groups with “no” or “unsure” responses was 50 and 52 years, respectively, there were more men 45 years or older (75%) in the “unsure” group (Table 1). The “yes” group had the...
Shabsigh R, et al. Awareness of erectile dysfunction

The highest mean age (59 years) and the greatest percentage of those aged 65 years or older (32%).

A correct ED diagnosis was more common for men who answered the screening question, “Do you have erectile dysfunction?” with the response of “yes” or “no.” Men who answered “yes” tended to have more severe ED, with 49% having severe (IIEF-EF score ≤10) and only 4% having no ED (IIEF-EF score ≥26). Men who answered “no” tended to have no or less severe ED, with only 6% having severe and 64% having no ED. The severity of ED in men who were unsure was almost equally distributed among the categories.

The mean number of ED risk factors was similar for all three screening response groups, with the mean ± SD of 2.9 ± 1.7 (range, 3–8) in the “yes” group, 2.6 ± 1.5 (range, 2–8) in the “no” group, and 3.2 ± 1.7 (range, 3–9) in the “unsure” group. Within each response group, hypertension, hypercholesterolemia, BMI ≥30 kg/m², and waist circumference ≥40 inches occurred most frequently. For each risk factor, an “unsure” response was most common (unsure: 48%–62%; no: 23%–39%; yes: 9%–27%) (Table 2).

The ED severity profiles for each response group for the individual comorbidities generally reflected the pattern observed in the overall population; most men who answered “no” to the screening question had no or mild ED, those who answered “yes” had mostly moderate and severe ED, and those who answered “unsure” had ED severity that was almost equally distributed across the ED severity categories. However, in the subgroups of men with coronary artery disease and those with diabetes, a higher proportion of men in the “unsure” groups had severe ED compared with the other comorbidities.

Discussion

This screening for ED among men with an ED-associated comorbidity and risk factors showed a high prevalence of the dysfunction diagnosed with IIEF-EF (71%), with more than half of these (54%) having moderate or severe dysfunction, 23% having mild-to-moderate dysfunction, and 23% having mild dysfunction. This supports recently reported results showing that even mild ED is an important indicator of risk for underlying disease associated with ED. Sexual dissatisfaction or “bother,” which can be assessed using the Erection Distress Scale or the Overall Satisfaction domain of the IIEF, may be an important part of the equation in a man’s self-perception of

<table>
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<tr>
<th>Table 1. Patient Characteristics by Response to the Screening Question, “Do You Have Erectile Dysfunction?”</th>
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<tr>
<td>Mean age, years (range)</td>
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<tr>
<td>Age distribution, n (%)</td>
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<td>18–44 years</td>
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<td>45–64 years</td>
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<td>≥65 years</td>
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<td>Race, n (%)</td>
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<td>Mean weight, kg (range)†</td>
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*Patients with both erectile dysfunction screening question and Erectile Function domain of the International Index for Erectile Function data.
†Data available for 971 men.

<table>
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<th>Table 2. Erectile Dysfunction Screening Response Within Each Risk Factor Group*</th>
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<td>Hypertension</td>
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<td>Hypercholesterolemia</td>
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<td>Obesity†</td>
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<td>Smoking</td>
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<td>Waist ≥40 inches</td>
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<td>Diabetes</td>
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<td>Depression</td>
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<td>LUTS</td>
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<td>Coronary artery disease</td>
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<td>Metabolic syndrome</td>
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*Patients with both erectile dysfunction question and Erectile Function domain of the International Index of Erectile Function data. BMI≥30 kg/m². BMI = Body mass index; LUTS = Lower urinary tract symptoms.
ED, regardless of the severity of the dysfunction.

In the current trial, the distribution of ED severity differed by answer to the erectile dysfunction screening question, with a majority of men who answered “yes” having mostly moderate to severe ED. Likewise, men who answered “no” to the screening question had mostly no or mild ED (IIEF-EF score ≥22), although 6% of men who answered “no” had severe dysfunction according to the IIEF-EF assessment (IIEF-EF score ≤10). Men who were unsure whether they had ED most often did have some degree of ED, but the severity was variable. Interestingly, a higher percentage of men in the “unsure” and overall groups with coronary artery disease or diabetes had severe ED compared with the other ED severity categories. The results for coronary artery disease are similar to those from a previous study showing 14% mild, 21% mild-to-moderate, 14% moderate, and 51% severe ED in men admitted to the emergency room with acute coronary syndrome and subsequently diagnosed with coronary artery disease. Likewise, a study in diabetic men with ED showed that these men had significantly lower scores on the IIEF-EF than men without diabetes, with a mean IIEF-EF score of 6 (severe ED).

A limitation of the trial design was that the reasons for men’s specific answers to the screening question were not further investigated. However, studies investigating treatment-seeking behavior of men with ED and those assessing men’s sexual attitudes and beliefs may serve to provide insight into how men react when they begin to experience ED as well as why some men may not recognize that they have ED.

Erectile dysfunction may produce a profound sense of loss. Men may try to make sense of the cause of their ED, which may include guilt or the pressures of business or work, or they may want to confirm that an existing medical problem is the cause rather than their feelings for their partner or their sexuality. Men frequently cited psychological stress, organic disease, and aging as causes for ED in a study of men’s sexual beliefs and attitudes. Men’s emotional reactions to ED include denial, embarrassment, depression, and acceptance. In keeping with this, men who have intermittent erection problems are less likely to seek treatment. The duration and severity of ED was also determined to be a factor in whether men sought treatment, suggesting that symptoms of ED may not be immediately recognized. When considered together, these factors suggested that for men who answered “no” or “unsure” in the current study and were identified as having ED by IIEF-EF score, the onset of symptoms of ED may have been poorly understood, not recognized as ED, or may have been denied.

Men who answered “yes” to the screening question and had ED apparently recognized that they had this condition, but had not been previously diagnosed. This suggested that these men may not have been interested in or were reluctant to seek resolution or treatment for their ED. Some treatment-seeking barriers that may explain why men with recognized ED do not seek treatment for it include the belief that ED is a natural part of aging, concern about the side effects of or not wanting to take drugs, the belief that nothing can be done about ED, fear that the underlying condition causing ED may be serious, and the cost of treatment. One study found that men would prefer to purchase ED medications anonymously or wanted the medication to be available without a prescription, suggesting that men may feel embarrassed about purchasing ED medications.

All men who were screened had comorbidities associated with ED. Pharmaceutical treatments for many of these ED-associated disorders are associated with sexual side effects, including ED. For example, fibrate derivatives used to treat hypercholesterolemia and diuretics and β-blockers for treatment of hypertension have been associated with ED. Drugs for LUTS and depression can also impact sexual health. Men who first experience ED after beginning medication to treat a comorbidity may not consider that they have ED, but may feel that their ED is an adverse effect of their treatment.

**Conclusions**

This study found that many men with risk factors associated with ED have the dysfunction, including 54% who had moderate or severe dysfunction; however, these men’s awareness of having ED was low. The results suggest that many men may not recognize that they have ED, may possibly deny it, or may not view symptoms of ED as a medical problem. Considering the impact that ED has on quality of life and that it may often respond to treatment, ED should be suspected and assessed in men with risk factors, such as cardiovascular disease, diabetes, and LUTS, regardless of their apparent level of awareness of ED.
Chronic Hepatitis B: A Major Health Problem in Asia

Chan HL, Jia J.

*J Gastroenterol Hepatol.* 2011;26 Suppl 1:131–137.

**Abstract**

Chronic hepatitis B virus (HBV) infection is a major health problem in the Asia-Pacific region. In the past decade, much progress has been made in the understanding and management of this disease. The introduction of universal vaccination has significantly reduced the incidence of perinatal infection in most of the Asia-Pacific countries. As the majority of the adult population have not been immunized at birth, we are still facing a large population of young HBV-infected patients in the coming two decades. The study of long-term longitudinal databases has provided deeper insight into the clinical significance of HBV DNA suppression, hepatitis B e antigen (HBeAg) seroconversion, and hepatitis B surface antigen (HBsAg) seroclearance in chronic hepatitis B. With a better understanding on the natural history of HBV infection, one can now stratify the risk of chronic hepatitis B patients for adverse clinical outcomes and use this to individualize management. The introduction of noninvasive assessment of liver fibrosis can potentially reduce the necessity of liver biopsy. There have also been great advances in the development of antiviral therapy in the past decade. However, the high cost of HBV antiviral drugs poses major challenges to health authorities in many Asia-Pacific countries. Properly performed cost-effective analysis and understanding on the best timing of stopping antiviral drugs will be important to facilitate the most appropriate allocation of resources.

Chronic hepatitis B virus (HBV) infection has been a major health concern in the Asia-Pacific region. Vaccination has considerably reduced the prevalence of perinatal infection in most Asia-Pacific countries; however, as the majority of adult population has not been immunized at birth, there will be a large population of HBV-infected patients in the next two decades.

**Hepatitis B Statistics**

- An estimated 2 billion people amounting to one third of the world population have been exposed to infection with hepatitis B virus (HBV).
- Globally, about 400 million people or about 6% of the world population have chronic hepatitis B virus infection.
- HBV causes 30% of cirrhosis worldwide, with hepatitis C virus (HCV) responsible for 27% of these cases.
- HBV causes 53% of hepatocellular carcinoma (HCC) worldwide, with hepatitis C virus (HCV) responsible for 25% of these cases.
- The number of people dying from HBV-related cirrhosis and HCC has been estimated to be 500,000.
- According to the Nationwide Disease Surveillance and Monitoring System, the HCC-related mortality in China was 15 per 100,000 in 1991 and 21 per
Clinical insight

Chronic HBV Infection: The Asian-Pacific Scenario

- HBV infection is highly endemic all over the world; the disease has a higher prevalence in Asia and the Pacific Islands, sub-Saharan Africa, the Amazon Basin and Eastern Europe.
- The Asia-Pacific region is home to nearly three quarters of chronic HBV carriers; 15% to 25% of these chronic carriers would die of HBV-related liver disease in due course.
- The Western Pacific region, defined by the World Health Organization (WHO) as including 37 countries including China, Japan, South Korea, Philippines, and Vietnam has less than one-third of the global population. However, it is responsible for almost 50% of all chronic HBV-infected individuals worldwide.
- Women have a lower seroprevalence of HBsAg as compared to that in men. The male-to-female ratio was 1.4:1 in mainland China, 1.3:1 in Thailand, and 1.1:1 in Hong Kong prior to the introduction of the HBV vaccine.

The prevalence of chronic HBV infection differs greatly among Asian countries.
- High-prevalence (>8%) regions include mainland China, Taiwan, Korea, Philippines, Thailand, Vietnam, and South Pacific island nations.
- Intermediate-prevalence (2%–7%) regions include central Asia, the Indian subcontinent, Indonesia, Malaysia, and Singapore.
- Low-prevalence regions (<2%) include Australia and New Zealand; but recently there has been a rise in prevalence due to immigrant population from high-prevalence countries.
- Intermediate-prevalence (2%–7%) regions include central Asia, the Indian subcontinent, Indonesia, Malaysia, and Singapore.

Phases of HBV Infection in Asian Patients

Perinatally acquired chronic hepatitis B is usually classified into three phases.
- Immune tolerance phase: This phase is characterized by hepatitis B e antigen (HBeAg) positivity, very high HBV DNA, normal alanine aminotransferase (ALT) levels, and minimal histologic injury. This lasts for the initial two to three decades of the infection.
- Immune clearance phase: Immune clearance results in decline in HBV DNA and rise in ALT levels. Patients, in whom immune clearance is unsuccessful or is prolonged, will have progressive liver fibrosis, which develops into cirrhosis of the liver.
- Low replicative phase: This phase follows successful immune clearance. It is marked by HBeAg seroconversion with positive anti-HBe antibodies and suppression of HBV DNA; ALT levels become normal. Patients in the low replicative phase have favorable prognosis.

Recent data has shed light on a fourth phase of HBV infection in Asian patients, called the immune escape phase in association with evolution of HBeAg-negative mutant forms of HBV. Patients in this phase have high HBV DNA with intermittent raised ALT levels. Showing similarity to European data, these HBeAg-negative patients with persistent viremia and

Safety and Efficacy of HD-03/ES* in Patients with Chronic Hepatitis B Virus Infection

Rajkumar JS, et al.

World J Gastroenterol.

An open prospective controlled clinical trial was conducted to investigate the safety and efficacy of the formulation HD-03/ES capsules in the management of patients with chronic hepatitis B infection. A total of 25 patients were recruited to the study and were given HD-03/ES, two capsules twice daily for 6 months. Clinical assessment of symptoms and signs were done using the “clinical observation table” once a month before and after the treatment. Biochemical investigations of total bilirubin, alanine transaminase (ALT), aspartate aminotransferase (AST), and serum protein for liver function tests were done every month after initiating treatment. Serum was analyzed for HBV markers for HBsAg, HbeAg, and HBV DNA at baseline, 4 and 6 months after therapy using enzyme-linked immunosorbent assay (ELISA) kits from Roche.

After 6 months of therapy with HD-03/ES, a significant reduction in ALT values from 66.5 ± 11.1 to 39.1 ± 5.2 (P < .01) and a significant HBsAg loss (52%, P < .001), HBeAg loss (60%, P < .05) and HBV DNA loss (60%, P < .05) was observed. Adverse effects were mild and never warranted withdrawal of the drug.

The results of this pilot study indicate that HD-03/ES might be a safe and effective treatment for chronic hepatitis B infection and a long-term multicentric comparator trial is warranted and under way.

*HD-03/ES is marketed as Liv.52 HB
biochemical activity are at a greater risk of cirrhotic complications and HCC.

Summary
The natural history of HBV infection is now more better understood than before. This has enabled categorization of patients into different risk groups, thereby allowing an individualized patient management.

Laughter Might be Good Medicine for Patients with Alzheimer Disease

Exposing patients with Alzheimer disease to “humor therapy” appears as effective as psychiatric drugs in reducing the agitation that often plagues those struggling with dementia, new Australian research suggests.

In a 3-month period, nursing home residents who actively participated in a weekly 2-hour clowning session involving music, mime, and humorous props showed a significant reduction in both physically and verbally aggressive behavior. The 20% plunge in overall agitation, which the team attributed to humor therapy, lasted for at least 14 weeks beyond the conclusion of the clowning program, the investigation team found.

Jean-Paul Bell (co-author of the study) and his colleagues sought to implement a “person-centered” therapeutic approach, coupling visual sight-gags such as mimicking a conversation through two tin cans alongside provocative and irreverent verbal humor to encourage active participation and reactions of the patient. The result was that the humor intervention worked well for pretty much everyone, particularly for the “highest-care” patients deemed most debilitated by dementia. As an added bonus, the impact was achieved without running any of the risk for serious side effects, including falling and premature death that have been previously associated with the prescription of antipsychotic drugs.

Bell and colleagues recently presented the findings at the National Dementia Research Forum, Sydney. The study authors noted that between 70% and 80% of dementia patients experience some form of agitation and distress, which can include bouts of wandering, screaming, and repetitive behaviors. To explore whether and how much humor might help, the authors focused on 399 nursing home residents with dementia or other “age-associated conditions” living in one of 35 facilities in the Sydney area. All the patients had lived in their respective facilities for at least 3 months. However, none were considered to be in an end-of-life situation or suffering from severe psychosis.

Humor sessions were performed weekly and to a large extent, the sessions relied on humorous improvisation skills, similar to those used by “clown doctors” performing for sick children. The goal was to lift the mood of the patients, while engaging them in both conversation and physical interaction. In addition, regular facility staff was partnered with these clowns, to continue to promote humor therapy between sessions.

Depression, quality-of-life, social engagement, and agitation behaviors were all assessed before beginning the therapy, at the end of 3-month program, and 26 weeks after beginning the therapy. Although humor therapy did not appear to affect mood or quality of life, it had a clinically significant impact on patient agitation, on par with what might be expected following administration of standard antipsychotic medications. However, while agitation itself remained lower 26 weeks following therapy launch, the boost in both happiness and positive behaviors seen during the program faded once the program ended. Nevertheless, the team suggested that humor therapy should become a first-line treatment choice for dementia patients suffering from agitation.

Clinical Insight

Researchers from Iran recently conducted two trials to evaluate the safety and effectiveness of ginger for treating female reproductive complaints. The first study compared ginger preparations to nonsteroidal anti-inflammatory drugs (NSAIDs) for relieving dysmenorrhea (painful or difficult menstruation). The second study evaluated ginger as a treatment for nausea and vomiting during pregnancy.

Dysmenorrhea is experienced by more than half of menstruating women. NSAIDs can be effective in relieving dysmenorrhea, but NSAIDs and other pain relievers commonly cause adverse side effects and are contraindicated in some people. Ancient medical texts refer to the use of ginger for relief of dysmenorrhea, but there are no published clinical trials to support its effectiveness. The researchers therefore conducted a study to compare the effects of ginger, mefenamic acid (a mild analgesic and fever-reducing NSAID used in some types of arthritis and for the relief of moderate short-term menstrual pain), and the NSAID ibuprofen on dysmenorrhea.

For the nonrandomized double-blind trial, the researchers recruited 150 female college students who were 18 years or older and had primary dysmenorrhea. The women completed a questionnaire that assessed menstrual characteristics and severity of pain. Those with moderate-to-severe dysmenorrhea were enrolled in the study and alternately allocated to one of the three groups: the ginger group, the mefenamic acid group, or the ibuprofen group. Depending on their assigned group, the women were instructed to take either four 250 mg capsules of ginger rhizome powder, four 250 mg capsules of mefenamic acid, or four 400 mg capsules of ibuprofen each day, beginning on the first day of their menstrual period and continuing for 3 days. After 3 days, women rated the severity of their dysmenorrhea, degree of pain relief, and their satisfaction with the treatment. Only one menstrual cycle was studied.

All 150 women completed the study. There were no significant differences in baseline characteristics among the three groups. Dysmenorrhea severity decreased in all three groups (P values not reported) after 3 days. Severity of symptoms, improvement in pain relief, satisfaction with the treatment, and compliance with capsules were not significantly different among the groups. None of the women reported any serious adverse side effects during the study.

Authors of the study concluded that ginger is as effective as mefenamic acid and ibuprofen in reducing menstrual pain. They also point out certain limitations of this study. The study subjects were alternately assigned to an experimental group rather than randomly assigned; however, baseline characteristics were similar among subjects in all three groups, and there is no indication of bias in group assignments. The study did not compare the effect of ginger on other menstrual symptoms, such as nausea, headaches, and fatigue. The scale used to rate dysmenorrhea severity was a verbal, 4-point scale, and authors suggest that the use of a 10-point visual analog scale or other standardized scale may detect more subtle differences in response among the experimental groups.

One issue that the authors did not address is the dosage of comparator drugs used in this study. It is not

Ginger in Nausea During Pregnancy

Sanskrit name/Indian name:  
Sunthi

English name:  
Ginger

Zingiber officinale
clear whether the doses selected for this study (1600 mg ibuprofen and 1000 mg mefenamic acid) are typical doses used for treatment of primary dysmenorrhea in the local population. In the United States, daily doses of 2400 to 3200 mg ibuprofen are commonly recommended for treatment of moderate or severe dysmenorrhea and may be more effective than the 1600 mg dose of ibuprofen used in this study. The recommended dose for mefenamic acid is 1500 mg/d. It is therefore unclear as to how much of a placebo effect occurred in this study. It would have been better if a placebo group had been included for comparison. Another limitation is that the study was very brief; typically, dysmenorrhea studies are conducted over a 3-month period. In addition to correcting the limitations discussed by the authors, future trials should assess the safety and efficacy of ginger during several menstrual cycles, investigate a range of ginger doses, and include populations of women other than young college students.

The second study assessed the effects of 1000 mg ginger administered in capsule form on the severity of nausea and vomiting in pregnant women. Up to 90% of women experience nausea and vomiting during pregnancy. Little is known about the safety of antinausea drugs during pregnancy, so some pregnant women turn to herbs or other complementary therapies for relief. Ginger has long been used to relieve stomach upset in the traditional medicines of many cultures.

This single-blind, randomized, placebo-controlled trial was conducted at prenatal clinics and Isfahan Shahid Beheshti Hospital in Isfahan, Iran. Seventy healthy, pregnant women who were less than 20 weeks of gestational age and who reported mild-to-moderate nausea with or without vomiting were enrolled in the trial. Women were randomly allocated to an experimental group or a matched control group. Women in the experimental group took four 250 mg capsules containing ginger root powder daily for 4 days. Women in the control group took four placebo capsules containing lactose daily for 4 days. Women were instructed to take a capsule four times daily (morning, noon, afternoon, and night).

Before starting the study, women rated the severity of their nausea and vomiting using a 10-point visual analog scale (VAS). Women were instructed to avoid fatty foods and eat smaller, more frequent meals during the study. Women completed a questionnaire each day and recorded the severity of their nausea on the VAS twice a day (at noon and at bedtime). On the fifth day, women were interviewed by a researcher to assess compliance with the dietary instructions and capsule use.

Of the 70 women who started the study, 67 completed the study (32 in the ginger group and 35 in the placebo group). There were no significant differences in nausea intensity between the two groups at baseline. Women in the ginger group reported significantly greater improvement in nausea than women in the placebo group (P<.05) during the 4-day trial. Nausea intensity declined in 84% of women in the ginger group and 56% of women in the placebo group (P<.05). The incidence of vomiting did not decrease significantly in the placebo group but decreased a significant 50% in the ginger group after 4 days (P<.05). None of the women reported any adverse side effects from the capsules. Compliance with the capsules was excellent in both groups; however, only about half of the women in each group reported complying with the dietary advice.

Authors concluded that daily treatment with 1000 mg of ginger is a safe and effective way to decrease the intensity of nausea as well as the incidence of vomiting during pregnancy. However, the authors’ conclusions that 1000 mg is the appropriate dose cannot be asserted given that this study was not a dose-ranging study. Also, authors’ conclusion that this dose is safe cannot be asserted since there has been no long-term, follow-up studies of the infants, and, given the small sample size, only very large changes in pregnancy outcomes would have been seen.

The results of this study are consistent with nine published randomized controlled trials, which have also evaluated the effectiveness of ginger for nausea and vomiting during pregnancy. In these trials, daily doses ranged from 1000 mg to 1500 mg and the ginger products included capsules containing ginger powder or ginger syrup, which is mixed with a beverage. Authors point out that the short duration of this trial is a limitation. Another limitation that authors did not discuss is whether the study was adequately blinded. Ginger capsules have a distinctive odor and flavor and it is possible that the people taking the placebo were aware that they had the placebo treatment. This could have affected to the study outcome. Future trials should assess the safety and effectiveness of ginger over a longer period of time, should improve study blinding, and enroll pregnant women with severe nausea and vomiting to expand the understanding of the effectiveness of ginger during pregnancy.

Abstracts

Cardiology

Revised Morphology and Hemodynamics of the Anorectal Vascular Plexus: Impact on the Course of Hemorrhoidal Disease

Aigner F, et al.

Aim: The aim of this study was to reassess the morphology and functional mechanisms of anorectal vascular plexus with regard to hemorrhoidal disease.

Materials and Methods: The anorectal vascular plexus was investigated in 17 anorectal and five hemorrhoidectomy specimens by means of conventional histology and immunohistochemistry. Vascular corrosion casts from two fresh rectal specimens were used for scanning electron microscopy. Transperineal color Doppler ultrasound (CDUS) with spectral wave analysis (SWA) was performed in 38 patients with hemorrhoidal disease and 20 healthy volunteers.

Results: The anorectal vascular plexus was characterized by a network of submucosal vessels exhibiting multiple thickened venous vessels separated by distinct sphincter-like constrictions. CDUS and SWA showed significant flow differences in peak velocities (6.8 ± 1.3 cm/s vs 10.7 ± 1.5 cm/s; \( P = .026 \)) and acceleration velocities (51 ± 4 ms vs 94 ± 11 ms; \( P = .001 \)) of afferent vessels between the control group and patients with hemorrhoidal disease.

Conclusions: Coordinated filling and drainage of the anorectal vascular plexus is regulated by intrinsic vascular sphincter mechanisms. Both morphological and functional failure of this vascular system may contribute to the development of hemorrhoidal disease.

Erectile Dysfunction as a Predictor for Subsequent Atherosclerotic Cardiovascular Events: Findings from a Linked-data Study

Chew KK, et al.

This study was conducted to investigate the role of erectile dysfunction (ED) as a predictor for atherosclerotic cardiovascular (CV) events subsequent to the manifestation of ED. The investigation involved retrospective study of data on a cohort of men with ED linked to hospital morbidity data and death registrations. By using the linked data, the incidence rates of atherosclerotic CV events subsequent to the manifestation of ED were estimated in men with ED and no atherosclerotic CV disease reported prior to the manifestation of ED. The risk of subsequent atherosclerotic CV events in men with ED was assessed by comparing these incidence rates with those in general male population.

On the basis of hospital admissions and death registrations, men with ED had a statistically significant higher incidence of atherosclerotic CV events (standardized incidence rate ratio [SIRR] 2.2; 95% CI, 1.9, 2.4). There were significantly increased incidence rate ratios in all age groups <70 years, with a highly significant downward trend with increase of age (\( P <.0001 \)) across these age groups. Younger age at first manifestation of ED, cigarette smoking, presence of comorbidities, and socio-economic disadvantage were all associated with higher hazard ratios for subsequent atherosclerotic CV events. These findings show that ED is not only significantly associated with but is also strongly predictive of subsequent atherosclerotic CV events. This is even more striking when ED presents at a younger age.
Abstracts

Dermatology

Erectile Dysfunction in Patients with Psoriasis: Increased Prevalence, an Unmet Need, and a Chance to Intervene

Goulding JM, et al.


This study was conducted to determine the prevalence and risk factors of ED in patients with psoriasis in comparison with a heterogeneous dermatology outpatient control group.

The researchers conducted a pilot study with a prospective observational cross-sectional design, recruiting consecutive adult male dermatology outpatients diagnosed with psoriasis or any other skin condition. Sexually active participants completed a questionnaire, a Dermatology Life Quality Index and validated five-item version of international index of erectile function (IIEF-5).

Fifty-three of 92 (58%) patients with psoriasis recorded an IIEF-5 score indicative of ED, compared to 64 of 130 (49%) control patients, reflecting an age-adjusted OR of 2.007 (95% CI, 1.088–3.701; *P* = .026). A multivariable logistic regression model indicated that increasing age and hypertension, but not a diagnosis of psoriasis, were independent risk factors for ED in this study population.

This study presents the largest survey of ED in patients with skin disease, and the first to posit the potential link between psoriasis, ED, and atherosclerosis. The researchers suggest that an assessment of sexual function should be a part of routine holistic care provided for dermatology outpatients, and highlight the need to screen for cardiovascular risk factors in those with documented ED.

Psoriasis Associated with Hepatitis C but not with Hepatitis B

Cohen AD, et al.

*Dermatology.* 2010;220(3):218-222.

This study was conducted to investigate the association between psoriasis and viral hepatitis. Psoriasis patients were compared to controls regarding the prevalence of viral hepatitis in a case-control study using logistic multivariate models. The study was performed utilizing the medical database of Clalit Health Services. The study included 12,502 psoriasis patients >20 years old and 24,287 age- and sex-matched controls. The prevalence of hepatitis C in patients with psoriasis was increased compared to the prevalence in controls (1.03 vs 0.56%; *P*<.001). In a multivariate analysis, psoriasis was associated with hepatitis C. An interaction with smoking was noted (smokers: OR = 1.93, 95% CI, 1.30–2.67; nonsmokers: OR = 2.22; 95% CI, 1.63–3.04). The prevalence of hepatitis B in patients with psoriasis was higher than in the controls (0.74 vs 0.56%; *P* = .043). However, in a multivariate analysis, psoriasis was not associated with hepatitis B (OR = 1.22; 95% CI, 0.93–1.60; *P* = .15). These observations support previous reports of an association between psoriasis and hepatitis C but not with hepatitis B. Physicians who care for patients with psoriasis should be aware of this possible association and consider screening patients with psoriasis for hepatitis C.
Gastroenterology

Bowel Habits in Hemorrhoid Patients and Normal Subjects

Johannsson HO, et al.

The aim of this study was to compare patients with hemorrhoids with a control population regarding functional bowel symptoms and anorectal complaints. One hundred consecutive patients who participated in a randomized study on hemorrhoidectomy completed a validated questionnaire on bowel and anorectal functional symptoms. Two hundred age- and gender-matched population-based control subjects and 100 gender-matched consecutive patients undergoing an orthopedic procedure served as two control groups, and completed the same questionnaire.

Bowel frequency was the same in all three groups, but only 37% of the patients described their bowel movements as normal, compared to 55% and 67% of the controls ($P<.001$). Up to 37% of the patients reported bloating, compared to 18% and 26% in the control groups. Abdominal pain associated with bowel evacuation was experienced by 34% of the patients but in 3% and 5% of the controls ($P<.001$). Excessive straining, feeling of incomplete evacuation, and repeated toilet visits were significantly more usual in the patients. Reduced feeling of well being and disturbed social life caused by bowel symptoms was often reported by patients but rarely in the control groups. Besides hemorrhoidal symptoms, many patients with grade 3 and 4 hemorrhoids have concomitant functional bowel symptoms, possibly associated with the irritable bowel syndrome. This knowledge might be important while selecting therapy for patients with hemorrhoids.

Intestinal Microbiota in Cirrhotic Patients with Hepatitis B Virus Infection

Lu H, et al.

This study was conducted to unravel the profile of intestinal microecological parameters in Chinese patients with asymptomatic carriage of hepatitis B virus (HBV), chronic hepatitis B, decompensated HBV cirrhosis, and health controls and to establish their correlation with liver disease progression. The researchers investigated fecal parameters, including population of fecal predominant bacteria and abundance of some virulence genes derived from Escherichia coli, Bacteroides fragilis, Clostridium difficile, and Clostridium perfringens in fecal crude DNA and some immunological parameters in extracts of all fecal samples.

Data analysis indicated that 16S rRNA gene copy numbers for Faecalibacterium prausnitzii, Enterococcus faecalis, Enterobacteriaceae, bifidobacteria, and lactic acid bacteria (Lactobacillus, Pediococcus, Leuconostoc, and Weissella) showed marked variation in the intestine of HBV cirrhotic patients. The bifidobacteria/Enterobacteriaceae (B/E) ratio, which may indicate microbial colonization resistance of the bowel, was decreased significantly in turn from 1.15 ± 0.11 in healthy controls, 0.99 ± 0.09 in asymptomatic carriers, and 0.76 ± 0.08 in patients with chronic hepatitis B to 0.64 ± 0.09 in patients with decompensated HBV cirrhosis (for all, $P<.01$). This suggests that B/E ratio is useful for following the level of intestinal microecological disorder in the course of liver disease progression. The data for virulence gene abundance suggested increased diversity of virulence factors during liver disease progression. Fecal secretory IgA and tumor necrosis factor-α in decompensated HBV cirrhotic patients were present at higher levels than in other groups, which indicate that a complicated autoregulatory system tries to achieve a new intestinal microecological balance.
The Impact of Hemorrhoidectomy on Sexual Function in Women

Lin YH, et al.


The purpose of this study was to explore the prevalence of sexual problems in post-hemorrhoidectomy females. The study consisted of a surgical group and a control group of women between 22 and 74 years of age, 39 with and 39 without hemorrhoidectomy. Female sexual function was evaluated using the female sexual function index (FSFI). The level of sexual function was calculated for each domain, and compared across domains and demographic variables, for each group. The prevalence of sexual dysfunction among the post-hemorrhoidectomy participants was 48.7% (19/39) and among the healthy women 7.7% (3/39). The average FSFI score was significantly lower in the surgical group (46.38 ± 28.13) than in the control group (65.69 ± 18.48; P = .001). All the FSFI domain scores, with the exception of the desire domain, were significantly lower for the surgical group relative to the healthy group (P < .05). Logistic regression analysis revealed that group (P = .001) and age (P = .013) were predictors of problems in female sexual functioning. This preliminary study shows that women who have had a hemorrhoidectomy are at higher risk of sexual function problems. The sexual function of women with hemorrhoidectomy should be evaluated to provide them with a better quality of life.

The Assessment of Sexual Functions in Women with Male Partners Complaining of Erectile Dysfunction

Cayan S, et al.


The aims of this prospective study were to compare sexual functioning between women with male partners complaining of erectile dysfunction (ED) (ED group; n = 38) and with male partners who have no ED (control group; n = 49), and also to investigate the effect of the treatment of male ED on female partner’s sexual function. Of the men with ED, 30 were treated with penile prosthesis implantation (n = 17) or oral sildenafil citrate (n = 13). Sexual arousal, lubrication, orgasm, satisfaction, pain, and total score were significantly lower in the ED group than in the control group, although sexual desire did not differ between the two groups (P = .515). The researchers investigated the effect of male ED on female sexual functions and found no statistically significant differences in the presence of organic type impotence, older age, and lower erection scores on the international index of erectile function (P = .53, P = .15, and P = .1, respectively). After the treatment of male ED, significant improvement in sexual arousal (P = .001), lubrication (P = .002), orgasm (P = .000), satisfaction (P = .000), and pain (P = .002) were noted in the women. These findings suggest that female sexual function is affected by male erection status and may improve after the treatment of male sexual dysfunction.
Hepatology

Risk Factors for Hepatocellular Carcinoma in a Cohort Infected with Hepatitis B or Hepatitis C

Walter SR, et al.

*J Gastroenterol Hepatol.* 2011.

The incidence of hepatocellular carcinoma (HCC) has increased in recent decades, a large proportion of which occurs among a population chronically infected with hepatitis B virus (HBV) or hepatitis C virus (HCV). However, risk factors for HCC among these high-risk groups require further characterization. The researchers conducted a population-based cohort study using HBV and HCV cases notified to the New South Wales (NSW) Health Department between 2000 and 2007. These were linked to cause of death data, HIV/AIDS notifications, and hospital records. Two hundred forty-two and 339 HCC cases were linked to HBV (n = 43,892) and HCV (n = 83,817) notifications, respectively. For both HBV and HCV groups, being male and increasing age were significantly associated with risk of HCC. Increasing comorbidity score indicated high risk while living outside urban areas was associated with lower risk. Hazard ratios for males were two to three times more as compared to females. For both HBV and HCV groups, cirrhosis, alcoholic liver disease, and interaction between the two were associated with significantly elevated risk. This large population-based study confirms known risk factors for HCC. The association with older age highlights the potential impact of HBV and HCV screening of at-risk groups and early clinical assessment. Additional research is required to evaluate the impact of improving antiviral therapy on HCC risk.

Erectile Dysfunction in Patients with Chronic Viral Liver Disease

Toda K, et al.


In patients with chronic liver disease (CLD), quality of life is generally accepted as poor, especially for physical function. However, sufficient data regarding erectile function has not been shown in patients with CLD. In this study, 117 Japanese patients (64 with chronic hepatitis [CH] and 53 with liver cirrhosis [LC]) were analyzed. The etiologies were hepatitis B virus (HBV) in 21, HCV in 94, and non-B non-C in two.

The incidence of ED was 85% in the total cohort with CLD, 78% in those with CH, and 92% in those with LC (P<.05 between CH and LC). ED was found in 50% of CLD patients under 50 years of age, in 79% aged 50–59, and in 100% aged over 60 (P, overall <.001). The scores for ED severity correlated with increasing grades of a modified Child-Pugh classification (P<.05). Simple regression analysis showed age (P<.01), physical function (P<.001), role physical (P<.001), and social functioning (P<.05), and serum albumin (P<.001) as significant determinants of ED. Multiple regression analysis identified age (P<.001) and serum albumin (P<.001) as independent significant factors that determined ED. These data clearly demonstrate that liver disease is the cause of ED in patients with CLD, and serum protein status could be relevant to this condition in these patients.
Infections

Acute Hepatitis: A Rare Complication of Epstein-Barr Virus Infection

Uluğ M, et al.


Infectious Mononucleosis (IM), a benign lymphoproliferative disease, is the best known clinical syndrome caused by Epstein-Barr virus (EBV). It usually resolves over a period of week or month without sequelae, but may occasionally be complicated by a wide variety of neurologic, hematologic, hepatic, respiratory, and psychological complications. In this report, the researchers describe a patient with acute hepatitis following EBV-IM in a previously healthy woman. A 26-year-old woman who presented with fever, generalized weakness, nausea, sore throat, yellowing of skin, and a generalized skin rash was admitted to their clinic. Tonsillar enlargement, pharyngeal erythema, palatal petechiae, lymphadenopathy, and jaundice were noted. Significant atypical lymphocytes (>10%) were seen on the peripheral blood smear. Liver function tests such as ALT (303 U/L), AST (172 U/L), ALP (193 U/L), and total bilirubin (7.3 mg/dL) were elevated. Serological tests for EBV infection were consistent with acute infection (EBV virus capsid antigen was reactive with IgM and IgG antibodies). The Monospot test was also positive. On the seventh day, liver function tests and bilirubin had risen to peak level and platelets were decreased. The patient was managed supportively and her critical condition improved and was finally stabilized. Although the prognosis for IM is very favorable, a variety of acute complications may occur.

Life-threatening Sepsis Following Treatment for Hemorrhoids: A Systematic Review

McCloud JM, et al.

*Colorectal Dis.* 2006;8(9):748-755.

Hemorrhoids are a common complaint with estimates suggesting a prevalence of 4% of the adult population. Treatments such as rubber band ligation (RBL), sclerotherapy, and excisional surgery have been in use for many years, and recently stapled hemorrhoidopexy, or procedure for prolapsing hemorrhoids (PPH) has gained acceptance. However, there have been consistent reports of severe sepsis, including a number of deaths. This review was conducted to assess the scale of the problem, and identify any predisposing factors, common presenting features, and treatment options in those who suffer these complications.

Twenty-nine papers were identified, reporting 38 patients. Of these, 17 had undergone RBL, 3 had sclerotherapy, 1 had cryotherapy, 10 had excisional surgery, and 7 had PPH. Ten died as a result of sepsis. The cases included 16 with perineal sepsis, 7 with retroperitoneal gas and edema, and 6 with liver abscesses. Common presenting features were urinary difficulties, fever, severe pain, septic shock, and leucocytosis. Most were managed by means of surgery, although a minority survived having received conservative therapy. With the exception of two patients (one of whom was human immunodeficiency virus positive and the other had drug-induced agranulocytosis) all were well prior to surgery. Although extremely uncommon, severe sepsis does occur posttreatment for hemorrhoids and all surgeons who treat such patients should be aware of the potential complications and alert to their presenting features.
Neurology

The Neurobiology of Psychogenic Erectile Dysfunction in the Spinal Cord

Sakamoto H.


It was recently reported that a previously unknown peptidergic system within the lumbosacral spinal cord that uses gastrin-releasing peptide (GRP) triggers erection and ejaculation in male rats. To determine whether acute severe stress could alter the male-specific GRP system, the researcher of this study used single prolonged stress (SPS) exposure in a putative rat model for PTSD. Exposure of male rats to SPS decreases the local content and axonal distribution of GRP in the lower lumbar spinal cord and results in an attenuation of penile reflexes in vivo. Pharmacological stimulation of GRP receptors remarkably restores penile reflexes in SPS-exposed male rats and in castrated male rats. The administration of a GRP agonist to these animal models interestingly induces spontaneous ejaculation in a dose-dependent manner. Furthermore, although the circulating level of androgens is normal 1 week after SPS exposure, there is a significant decrease in the expression of androgen receptor protein in lumbar segments three and four of the spinal cord. This might make the spinal center less responsive to androgens. In this report, a recently identified spinal GRP system, which could be vulnerable to stress and controls male reproductive function, provides new insights into the clinical treatment of psychogenic erectile dysfunction triggered by stress and psychiatric disorders.

Depression in Patients with Nonalcoholic Fatty Liver Disease and Chronic Viral Hepatitis B and C

Weinstein AA, et al.


The purpose of this study was to determine the prevalence of depression in chronic liver disease (CLD) patients (non-alcoholic fatty liver disease (NAFLD), Hepatitis B (HBV), and Hepatitis C (HCV)) and to identify potential clinical and laboratory correlates of depression in these patients.

The researchers used a database of CLD patients that contains extensive clinical (including self-reported depression) and laboratory data for each patient. They compared the prevalence of depression in patients with HBV, HCV, and NAFLD. They also used regression models to find independent predictors of depression in these patients. Out of 878 CLD patients, 207 (23.6%) were diagnosed for depression (NAFLD 27.2%, HCV 29.8%, and HBV 3.7%). Examination of predictors of depression differed by the type of chronic liver disease. For NAFLD, independent predictors of depression were the presence of hypertension, smoking, history of lung disease, being female, and non-African American. For HBV patients, the only independent predictor of depression was excessive alcohol consumption (defined as >10 g/d), while for HCV patients, independent predictors were being female and non-Asian, fatigue, and excessive alcohol intake.

This study demonstrates that individuals with NAFLD and HCV have a higher prevalence of depression than HBV patients and the rates of depression reported for general population. The most consistent correlates of depression status in CLD patients are being female and excessive alcohol consumption.
Ophthalmology

How Does Hypertension Affect Your Eyes?

Bhargava M, et al.

*J Hum Hypertens.* 2011.

Hypertension has profound effects on various parts of the eye. Classically, elevated blood pressure results in a series of retinal microvascular changes called hypertensive retinopathy, comprising generalized and focal retinal arteriolar narrowing, arteriovenous nicking, retinal hemorrhages, microaneurysms and, in severe cases, optic disc and macular edema. Studies have shown that mild hypertensive retinopathy signs are common and seen in nearly 10% of the general adult nondiabetic population. Hypertensive retinopathy signs are associated with other indicators of end-organ damage (e.g., left ventricular hypertrophy and renal impairment) and may be a risk marker of future clinical events, such as stroke, congestive heart failure, and cardiovascular mortality. Furthermore, hypertension is one of the major risk factors for development and progression of diabetic retinopathy, and control of blood pressure has been shown in large clinical trials to prevent visual loss from diabetic retinopathy. In addition, several retinal diseases such as retinal vascular occlusion (artery and vein occlusion), retinal arteriolar emboli, macroaneurysm, ischemic optic neuropathy, and age-related macular degeneration may also be related to hypertension; however, there is as yet no evidence that treatment of hypertension prevents vision loss from these conditions. In management of patients with hypertension, physicians should be aware of the full spectrum of the relationship of blood pressure and the eye.

Correlation between Penile Cavernosal Artery Blood Flow and Retinal Vascular Findings in Arteriogenic Erectile Dysfunction

Emarah AM, et al.


Arteriogenic erectile dysfunction (ED) is a target organ disease of atherosclerosis, and therefore might be a predictor of systemic atherosclerosis. Being systemic, it might be possible to evaluate the extent of atherosclerosis from retinal vascular findings. The researchers investigated the possible correlation between penile cavernosal artery blood flow and retinal vascular findings in patients with arteriogenic ED.

Sixty patients with ED were divided according to the peak systolic velocity (PSV) in their penile cavernosal arteries into two groups; Group A included 30 patients with PSV less than 25 cm/s, and Group B included 30 patients with PSV more than 35 cm/s. Blood flow in the penile cavernosal artery was measured with color Doppler ultrasonography. All patients were assessed by ocular fundus examination under amyndriatic conditions to evaluate retinal vascular atherosclerotic changes using Hyman’s classification.

Evidence of retinal vascular atherosclerotic changes was found in 19 patients (63.3%) in Group A and in 10 patients (33.3%) in Group B.

This study confirms the possibility of predicting penile arterial vascular status in patients with ED from their retinal vascular findings by using amyndriatic simple, practical funduscropy.
Orthopedics

Male Sexual Dysfunction after Pelvic Fracture
Metze M, et al.


A cross-sectional, retrospective study of male sexual function was conducted to assess multiple aspects of male sexual function after pelvic fracture. Patients admitted with traumatic pelvic fracture between January 1995 and June 2001 were included. One hundred and two patients were invited by mail. After performing a standardized clinical examination including an interview, the patients were asked to answer a questionnaire at home. Sexual dysfunction was classified as erectile dysfunction (ED), ejaculatory dysfunction, sensory loss in genital region, and pain during sexual activity. ED was assessed by International Index of Erectile Function (IIEF). The pelvic injury was classified using Tile’s classification.

Complete data of 77 men were available (age: 35 ± 13). A total of 47 patients (61%) reported limitations in sexual function. Persistent ED was found in 15 patients (19%). The patient’s report of ED could be verified by a low IIEF score in 14 cases. Injury patterns, which may increase the incidence of sexual dysfunction, could be identified. A ruptured symphysis appeared to bear a risk of temporary ED. Comparing compression and distraction in type B injuries, patients with distraction injury showed more severe sexual function. Posterior ring disruptions seemed to increase the risk of persistent problems, possibly caused by nerve damage.

This study emphasizes that major pelvic trauma may impair sexual function in men. The IIEF questionnaire might be considered to identify patients who need further medical evaluation.

Prevalence of Hepatitis B Surface Antigen in Patients with Ankylosing Spondylitis and its Association with HLA-B27

*Rheumatol Int.* 2011.

This study was conducted to investigate the prevalence of hepatitis B surface antigen (HBsAg) in patients with ankylosing spondylitis (AS) from south China and to evaluate its association with human leukocyte antigen, HLA-B27. The prevalence of HBsAg was retrospectively investigated in 439 patients with AS, 606 age- and sex-matched general individuals, 172 patients with other spondyloarthropathy (SpA), 698 patients with rheumatoid arthritis (RA), and 220 patients with osteoarthritis (OA). The positive rate of HBsAg in AS group was compared with those of the general population group and other disease groups, respectively, and the prevalence of HBsAg was compared between HLA-B27-positive and HLA-B27-negative patients with AS. The positive rate of HBsAg in AS patients, general population, other SpA, RA, and OA patients were 25.39%, 12.87%, 14.53%, 9.60%, and 8.18%, respectively. The HBsAg prevalence of AS group was statistically higher than those of any other groups (*P* < .05). The prevalence of HBsAg in HLA-B27-positive and HLA-B27-negative AS patients were 26.68% and 14.49%, respectively, the positive rate of HBsAg in HLA-B27-positive AS patients was statistically higher than that of HLA-B27-negative AS patients (*P* < .05). The prevalence of HBsAg in AS patients was higher than those in general population, patients with other SpA, RA, and OA. The high HBsAg prevalence in AS patients might be associated with their high frequency of HLA-B27 gene.
Predictors of Outcome in Acute-on-Chronic Liver Failure in Children
Lal J, et al.

*Hepatol Int.* 2010.

Acute-on-chronic liver failure (ACLF) is associated with a high mortality rate in the absence of liver transplantation and there is limited data on predictors of survival in ACLF in children. This study prospectively investigated the predictors of outcome of ACLF in children.

A total of 31 children between 1 and 16 years who fulfilled the criteria for ACLF were considered and were evaluated for etiology, diagnosis, and severity of ACLF. For grading of organ dysfunction, the sequential organ failure assessment (SOFA) score was calculated. Of the 31 children who fulfilled the criteria for ACLF, the common underlying chronic liver diseases (CLD) were autoimmune hepatitis (AIH) in 41.9% and Wilson disease in 41.9% of the patients. Super infection with hepatitis A virus (HAV) (41.9%) was the most common etiology of acute deterioration. To find the best predictor for outcome, linear regression analysis was performed. Multivariate analysis revealed that the SOFA score and the International Normalized Ratio (INR) were predictors of survival. Six (19.4%) patients died. Causes of death were multiorgan failure in four and liver failure in two patients. The mortality in ACLF is 19.4% and the causes of death were multiorgan failure and liver failure. The SOFA score and INR were predictors of outcome of ACLF in children.

Breastfeeding of Newborns by Mothers Carrying Hepatitis B Virus: A Meta-analysis and Systematic Review
Shi Z, et al.


The aim of this study was to perform a systematic review of prospective studies to confirm the role of breastfeeding in mother-to-child transmission (MTCT) of hepatitis B virus (HBV). A database was constructed from major databases and through contact with experts in this field from 1990 to 2010. Data regarding HBV intrauterine infection, MTCT, maternal blood and breast milk infectiousness, infant immunoprophylaxis methods and response, and adverse events were the main outcome measures.

Ten clinical controlled trials, involving 751 infants in the breastfeeding group and 873 infants in the non-breastfeeding group, were considered. As indicated by infant peripheral blood, hepatitis B surface antigen or HBV DNA positivity at 6 to 12 months of age, the odds ratio of MTCT of HBV in the breastfeeding group compared with that in the nonbreastfeeding group was 0.86 (95% CI, 0.51–1.45) (from 8 clinical controlled trials, \( P = .56; I(2) = 0\% , \ P = .99\)). The odds ratio of development of hepatitis B surface antibodies in the breastfeeding group compared with that in the nonbreastfeeding group was 0.98 (95% CI, 0.69–1.40) (from 8 clinical controlled trials, \( P = .93; I(2) = 0\% , \ P = .99\)). Breastfeeding after proper immunoprophylaxis did not contribute to MTCT transmission of HBV.
Herb Profile: *Aloe vera*

**Introduction**

*Aloe* species is found throughout the tropical and warm regions worldwide. Aloe is thought to have originated in North Africa or the Nile region in Sudan. There are approximately 360 species and subspecies of succulent plants (herbs, shrubs, and trees) in the genus *Aloe*, distributed in Africa, Arabian Peninsula, and certain islands of the Indian Ocean. However, wild origin of *Aloe vera* is uncertain. The commercially significant Aloes are perennials with 15 to 30 fleshy leaves up to 1.5 feet long, 3 to 4 inches across the base, and with saw teeth marking the margins of leaves.

**History and Cultural Significance**

*Aloe*’s use dates back almost 6000 years. Its uses were first documented on a Mesopotamian clay tablet dating from 2100 BCE and the Ebers Papyrus (ca. 1550 BCE), discovered in Egypt in 1873, listing at least 12 *Aloe*-containing preparations for treating internal and external ailments. In the 1st century CE, the Greek physician Dioscorides (ca. 40–90) recommended it for boils, chapping, genital ulcers, hair loss, hemorrhoids, inflammation, and mouth irritation. Pliny the Elder (ca. 23–79 CE) and Galen (ca. 130–200 CE) used Aloe to treat wounds and gastrointestinal disorders. Additional ancient medicinal uses include treatment for acne, arthritis, burns, dermatitis, headache, high blood pressure, indigestion, peptic ulcers, pruritus, and psoriasis. The Egyptian queens Neferiti and Cleopatra used it as a beauty aid, and it was used for embalming according to Pliny the Elder.

Various species of *Aloe* have long been used to treat constipation, specifically with the anthraquinone-containing latex found in cells inside the leaves. In the United States, *Aloe* was included in the first edition of United States Pharmacopoeia (USP) of 1820, and it remains official in the 33rd revision of the USP in 2010 as an official laxative drug.

Inner leaf of *Aloe vera*, often called “gel,” and leaf juice have been used externally for posttreatment of dermabrasion (such as acne scars, tattoos, and fine wrinkles) to promote wound healing and alleviate psoriasis. In cosmetics, *Aloe vera* juice and gel is added to moisturizers, cleansers, shampoos, suntan lotions, and sunburn treatments. Although other species of *Aloe* are used globally in various products, *Aloe vera* is believed to be the most widely used species throughout the world.

**Modern Research**

**Effect of *Aloe vera* on psoriasis**

At least three human clinical studies have been conducted to evaluate the efficacy of *Aloe vera* in psoriasis. In a randomized, comparative, double-blind, 8-week study including 80 patients, it was observed that topical *Aloe vera* cream was more effective than 0.1% triamcinolone acetonide in mild to moderate cases of psoriasis. In another double-blind placebo controlled study, 60 patients with psoriasis were self-treated with a 0.5% *Aloe* extract in a hydrophilic cream or placebo 3 times daily for 5 days.

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*Sanskrit name/Indian name:* Ghrita-kumari/Kanya/Kumari

*English name:* Barbados Aloe
Special feature

per week for 4 weeks. After 16 weeks, symptoms of psoriasis were cleared in 25 out of 30 patients treated with Aloe cream, compared to 2 out of 30 patients in the placebo group.

Effect of Aloe vera on lichen planus

Two studies reported the effectiveness of Aloe against lichen planus, a chronic skin condition characterized by an itchy rash. In one randomized, double-blind, placebo-controlled study, including 54 patients with oral lichen planus, 22 out of 27 patients treated with Aloe vera gel had a good response after 8 weeks of treatment (compared to 2 out of 27 in the placebo-treated group), and 2 had complete clinical remission.

In another randomized, double-blind, placebo-controlled study comprising 34 female patients with vulval lichen planus, 14 out of 17 patients treated with Aloe vera improved by at least 50% after 8 weeks of treatment, as compared to improvement in only 1 out of 17 patients in the placebo group.

Effect of Aloe vera on burns

In a randomized controlled study, 30 patients with two same site second degree burns that had occurred within 24 hours were treated twice daily with spray-dried Aloe vera powder on one site and silver sulfadiazine (SSD) cream on the other. The Aloe-treated sites healed approximately 3 days sooner (mean 15.9 ± 2 days) than the SSD-treated sites.

In a meta-analysis of four studies that explored the effects of Aloe vera on burns with duration of wound healing as an outcome measure, it was observed that despite differences in products and dosages used, Aloe might speed up the wound healing process and increase the rate of healing success in first and second degree burns.

Anti-inflammatory property of Aloe vera

In 2008, a randomized, double-blind, placebo-controlled study explored the anti-inflammatory properties of Aloe leaf gel on 40 volunteers who were irradiated with a 1.5-fold minimal erythema dose of UVB. The test areas were treated on two subsequent days with 97.5% Aloe leaf gel, 1% hydrocortisone in placebo gel, or 1% hydrocortisone in cream. The Aloe gel significantly reduced UV-induced erythema after 48 hours, performing better than the hydrocortisone in gel but not as good as the hydrocortisone in cream.

An open comparison study evaluated dry-coated Aloe vera gloves on participants who were factory assembly-line workers with repeated occupation-induced superficial skin trauma. After 7 to 17 days (mean time 10.4 days), marked improvement in skin quality (erythema, fissures, and excoriation) of the gloved hands were observed. There was no improvement in the nongloved hands of any participant.

In 2002, a preliminary open, noncomparative study observed that the crude Aloe vera leaf gel was as effective in the treatment of scabies as was a benzyl benzoate lotion. A 2006 study concluded that freeze-dried Aloe extract added to cosmetic formulations improves skin hydration.

Some other studies have shown that Aloe vera has the potential to prevent kidney stone formation in children and reduce histological disease activity in patients with mild to moderate ulcerative colitis.

A number of studies have also been conducted using acemannan, an acetylated polymannose identified in the 1980s as a primary active component in Aloe vera leaf gel. Clinical studies have shown its efficacy in acceleration of wound healing in postdermabrasion, partial thickness of wounds, and pressure ulcers. Freeze-dried acemannan was also shown to be effective against painful dry socket treatment as a result of dental procedure complications. Acemannan has also shown benefit in the reduction in AIDS symptoms, synergism and/or no interference with azidothymidine, in improved quality of life and morphologic alterations in HIV patients, and in preventing virus penetration and stimulating the immune system. Acemannan has also shown promise in in vitro and in vivo studies for managing cancer with no toxicity or adverse side effects. However, some Aloe processing techniques remove much if not all of the acemannan, possibly explaining some of the inconsistent effects of commercial Aloe products.

In 1998, the US National Toxicology Program (NTP) published an executive summary on Aloe vera gel, raising safety concerns about oral Aloe products due to the mutagenic properties of one of its anthraquinone constituents, 1,8-dihydroxanthracene. However, the summary also stated that most Aloe products sold for oral consumption in dietary supplements have reduced quantities of 1,8-dihydroxanthracene.

Aloe vera, as a component of dietary supplement products, is the subject of ongoing research by FDA Division of Biochemical Toxicology.

Future Outlook

The main cultivation areas for Aloe vera include Africa (eg, KwaZulu-Natal), the West Indies, The Netherland Antilles (Curaçao), South
Antibiotic Overuse Reduced Without Restricting Availability

A multidisciplinary antimicrobial stewardship program (ASP) at a tertiary care hospital has reduced antibiotic use in that institution by one quarter. In addition, the use of simple innovative changes to prescribing practices reduced the development and transmission of multidrug resistant (MDR) organisms over a 3-year period.

The ASP was accompanied by reduction in hospital costs and improvement in patient care. A vital aspect of the ASP was not to restrict antibiotics, Kimberly Leuthner infectious disease clinical specialist at the University Medical Center of Southern Nevada, Las Vegas, reported at the 51st Interscience Conference on Antimicrobial Agents and Chemotherapy.

Dr Leuthner said that the overuse of antibiotics imposes selective pressure on bacteria, leading to MDR organisms. Elevated rates of MDR pathogens, high rates and long duration of therapy, and excessive expense within the medical center led staff in 2006 to implement a multidisciplinary ASP involving infection control, microbiology, and pharmacy departments and functions.

The ASP included the evaluation of medication use for targeted drugs, a 10-day “stop protocol” for antimicrobial agents, expansion of a hospital-wide antibiogram, prevention strategies, and a continuing education program for nurses and physicians.

The ASP team decided not to restrict antibiotic prescribing, but to allow their use with education and de-escalation guidance. Drug use was monitored and adjusted for patient census by expressing use as doses per 1000 patient-days.

Dr Leuthner reported that antibiotic use decreased by 26.6%, and attributed the decrease to better compliance with medication use criteria and to the influence of the 10-day stop protocol. Stopping antimicrobial drugs sooner was associated with a significant decrease in the isolation of MDR pathogens ($P = .02$).

The researchers said that through the efforts of the infection control department, isolates of Acinetobacter species, *Pseudomonas aeruginosa*, and methicillin-resistant *Staphylococcus aureus* (MRSA) have decreased sharply by 30.7%, 24.6%, and 25.5%, respectively. The budget for antimicrobial drugs dropped by about 40% over a period of 3 years.

Source: Presented at 51st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), September 27, 2011.
Clinical Practice Pearls

Management of Chronic Hepatitis B
European Association for the Study of the Liver Clinical Practice Guidelines

Introduction
The understanding of natural history of hepatitis B virus (HBV) infection and the potential for therapy of the resultant disease has improved. Several new and effective antiviral agents have been evaluated and licensed since the EASL (European Association for the Study of the Liver) International Consensus Conference on hepatitis B held in 2002. The objective of these EASL Clinical Practice Guidelines (CPGs) is to update recommendations for the optimal management of chronic hepatitis B (CHB).

Pretherapeutic Assessment of Liver Disease
As a first step, the causal relationship between HBV infection and liver disease has to be established and an assessment of the severity of liver disease needs to be performed.

- The assessment of the severity of the liver disease should include: biochemical markers, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase, prothrombin time, and serum albumin; blood counts; and hepatic ultrasound. Usually, ALT levels are higher than those of AST. However, when the disease progresses to cirrhosis, the ratio may be reversed. A progressive decline in serum albumin concentrations and prolongation of the prothrombin time, often accompanied by a drop in platelet counts, are characteristically observed after cirrhosis has developed.
- HBV DNA detection and HBV DNA level measurement is essential for the diagnosis, decision to treat, and subsequent monitoring of patients. Follow-up using real-time PCR quantification assays is strongly recommended because of their sensitivity, specificity, accuracy, and broad dynamic range.
- Other causes of chronic liver disease should be systematically looked for including coinfection with HDV, HCV, and/or HIV. Comorbidities, including alcoholic, autoimmune, metabolic liver disease with steatosis or steatohepatitis should be assessed.
- A liver biopsy is recommended for determining the degree of necroinflammation and fibrosis in patients with either increased ALT or HBV DNA levels >2000 IU/mL (or both) since hepatic morphology can assist the decision to start treatment. Biopsy is also useful for evaluating other possible causes of liver disease such as steatosis or steatohepatitis. A liver biopsy is usually not required in patients with clinical evidence of cirrhosis or in those in whom treatment is indicated irrespective of the grade of activity or the stage of fibrosis.

Goal of Therapy
The goal of therapy for hepatitis B is to improve quality of life and survival by preventing progression of the disease to cirrhosis, decompensated cirrhosis, end-stage liver disease, HCC, and death. This goal can be achieved if HBV replication can be suppressed in a sustained manner, the accompanying reduction in histological activity of chronic hepatitis lessening the risk of cirrhosis and decreasing the risk of HCC in noncirrhotic patients and probably also, but to a lesser extent, in cirrhotic patients. However, HBV infection cannot be completely eradicated due to the persistence of covalently closed circular DNA (cccDNA) in the nucleus of infected hepatocytes.

End Points of Therapy
Therapy must reduce HBV DNA to as low a level as possible, ideally below the lower limit of detection of real-time PCR assays (10–15 IU/mL), to ensure a degree of virological suppression that will then lead to biochemical remission, histological improvement, and prevention of complications. If real-time PCR is unavailable, HBV DNA should...
be measured by the most sensitive assay possible.

- In HBeAg-positive and HBeAg-negative patients, the ideal end point of therapy is sustained HBsAg loss with or without seroconversion to anti-HBs. This is associated with a complete and definitive remission of the activity of chronic hepatitis B and an improved long-term outcome.

- In HBeAg-positive patients, durable HBe seroconversion is a satisfactory end point because it has been shown to be associated with improved prognosis.

- In HBeAg-positive patients who do not achieve HBe seroconversion, and in HBeAg-negative patients, a maintained undetectable HBV DNA level on treatment with nucleoside/nucleotide analogs (NUCs) or a sustained undetectable HBV DNA level after interferon therapy is the next most desirable end point.

Indications for Treatment

The indications for treatment are generally the same for both HBeAg-positive and HBeAg-negative CHB. This is based mainly on the combination of three criteria:

- Serum HBV DNA levels
- Serum aminotransferase levels
- Histological grade and stage

Patients should be considered for treatment when HBV DNA levels are above 2000 IU/mL (ie, approximately 10,000 copies/mL) and/or the serum ALT levels are above the upper limit of normal (ULN) for the laboratory, and liver biopsy (or noninvasive markers when validated in HBV-infected patients) shows moderate to severe active necroinflammation and/or fibrosis using a standardized scoring system (eg, at least grade A2 or stage F2 by METAVIR scoring).

Indications for treatment must also take into account age, health status, and availability of anti-viral agents in individual countries.

The following special groups of patients should be considered:

- Immunotolerant patients. Most patients under 30 years of age with persistently normal ALT levels and a high HBV DNA level (usually above 107 IU/mL), without any suspicion of liver disease and without a family history of HCC or cirrhosis do not require immediate liver biopsy or therapy. Follow-up is mandatory.

- Patients with mild CHB. Patients with slightly elevated ALT (less than two times ULN) and mild histological lesions (less than A2F2 with METAVIR scoring) may not require therapy. Follow-up is mandatory.

- Patients with compensated cirrhosis and detectable HBV DNA may be considered for treatment even if ALT levels are normal and/or HBV DNA levels are below 2000 IU/mL (ie, approximately 10,000 copies/mL).

- Patients with decompensated cirrhosis require urgent antiviral treatment. Rapid and profound viral suppression and efficacious prevention of resistance are particularly needed in this group. Significant clinical improvement can be associated with control of viral replication, but patients with very advanced liver disease may not always benefit if treated at this late stage and should be considered for liver transplantation.

Treatment Failure

It is important to distinguish between primary nonresponse (less than 1 log₁₀ drop of HBV DNA at 12 weeks), partial virological response (detectable HBV DNA on real-time PCR assay during continuous therapy), and virological breakthrough due to antiviral drug resistance.

- Primary nonresponse. In patients with primary nonresponse, it is important to check for compliance. In a compliant patient with a primary nonresponse, identification of possible HBV resistance mutations can formulate a rescue strategy that must reasonably be based on an early change to a more potent drug that is active against the resistant HBV variant.

- Partial virological response. Partial virological response may be encountered with all available NUCs. It is important to check for compliance.

- Virological breakthrough. Virological breakthrough in compliant patients is related to viral resistance. Resistance is associated with prior treatment with NUCs (such as lamivudine, adefovir, telbivudine, and emtricitabine) or, in treatment-naïve patients, with high baseline HBV DNA levels, a slow decline in HBV DNA, and partial virological response during treatment. Resistance should be identified as early as possible before clinical breakthrough (increased ALT) by means of HBV DNA monitoring, and if possible identification of the pattern of resistance mutations should be used to adapt therapeutic strategies. Indeed, clinical and virological studies have demonstrated the benefit of
an early treatment adaptation, as soon as viral load increases.

- In case of resistance, an appropriate rescue therapy should be initiated with the most effective antiviral effect and the minimal risk to induce multiple drug-resistant strains. Therefore, adding-on a second drug without cross-resistance is the only efficient strategy.

**Unresolved Issues and Unmet Needs**

- Improve knowledge of the natural history, in particular of immunotolerant patients, with long-term follow-up of cohorts: Experimental studies to provide more definite prognostic information, and biomarkers to determine prognosis and indications for treatment.

- Develop and assess new therapeutic approaches, particularly immunomodulatory therapies to enhance loss of HBeAg and HBsAg and subsequent seroconversion.

- Assess the role of indirect markers (serum and biophysical) to assess the severity of liver disease and for the follow-up of treated and untreated patients.

- Assess the role of HBV genotype to determine prognosis and response to therapy and the risk of resistance.

- Better define monitoring algorithms: timing of HBV DNA measurement with the new generation of NUCs with a high genetic barrier to resistance; role of genotypic resistance assays in adapting therapy.

- Assess long-term impact of therapy on the prevention of cirrhosis and its complications and HCC.

- Develop effective and optimum treatment for HDV coinfection.

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**Women Lose Patella Cartilage at a Faster Rate Than Men: A 4.5-Year Cohort Study of Subjects with Knee Osteoarthritis**

Patellofemoral knee osteoarthritis (OA) is a common disease and a significant cause of knee pain; however, few data have examined longitudinal change at the patellofemoral joint. The aim of this study was to examine factors affecting change in patella cartilage over a longer time period than previously examined.

Longitudinal study of 77 subjects (58% female) with knee OA underwent magnetic resonance imaging (MRI), with a repeat MRI of the same knee obtained approximately 4.5 years later. The main outcome measures were annual change in patella cartilage volume and annual percentage change over 4.5 years.

After adjusting for age, gender, body mass index (BMI), and patella bone volume at baseline, cartilage change was observed at the rate of 2.5% (95% CI, 2.0, 3.0) per annum over 4.5 years. Cartilage was lost at a higher rate in women compared to men after accounting for age, BMI, or bone volume at baseline (3.3% vs 1.4%, respectively, \( P = .03 \)). Increased patella bone volume was associated with increased patella cartilage loss \( (P = .02) \). No measures of radiographic severity of disease affected change in cartilage volume. The increased rate of cartilage loss in women may contribute to the increased prevalence of disease, although the underlying mechanism requires further study. Increased patella bone volume was also associated with increased patella cartilage loss. Whether this is due to biomechanical factors will need to be determined.

Clinical Insight

Drug Alert

Sudden Sensorineural Hearing Loss Associated with Vardenafil

The phosphodiesterase type 5 (PDE-5) inhibitors—sildenafil, vardenafil, and tadalafil—are used primarily in erectile dysfunction, but sildenafil is also indicated for pulmonary hypertension. Common adverse effects of vardenafil include headache, flushing, nasal congestion, dyspepsia, and nausea. Recently, PDE-5 inhibitors have been associated with adverse vision effects and emerging evidence now indicates that they may also be responsible for hearing changes and hearing loss. The researchers describe a patient who developed unilateral sudden sensorineural hearing loss possibly related to the use of vardenafil for erectile dysfunction. According to the researchers, only one other case of hearing loss related to this drug class had been published. A 57-year-old male patient came to the emergency department with right-sided mild-to-moderate hearing loss in 500–3000 Hz range (confirmed by audiogram), which occurred after ingestion of vardenafil. The patient was hospitalized 2 days later for administration of intravenous dexamethasone, followed by oral prednisone. The patient reported that his hearing had improved on the fourth hospital day and was discharged 3 days later, continuing to taper the prednisone on an outpatient basis. A repeat audiogram after 10 days of corticosteroid therapy confirmed that his hearing in the 500–3000 Hz range was within normal limits. Use of the Naranjo adverse drug reaction probability scale indicated a possible (score of 3) adverse reaction of sudden sensorineural hearing loss associated with vardenafil consumption. The researchers also performed an analysis of hearing loss cases related to PDE-5 inhibitors in the United States Food and Drug Administration’s Adverse Event Reporting System database to compare the characteristics of the patient with those of other reported adverse event cases. Based on the temporal relation of the sudden sensorineural hearing loss to this patient’s drug consumption, the researchers propose that the vardenafil is a likely cause of the hearing loss. This case provides further evidence that PDE-5 inhibitor consumption should be considered as a possible cause in patients presenting with sudden sensorineural hearing loss.

Regular Nonsteroidal Anti-Inflammatory Drug Use and Erectile Dysfunction
Gleason JM, et al.

Objective: Previous data suggest a potential relationship between inflammation and erectile dysfunction. If it is causal, nonsteroidal anti-inflammatory drug use should be inversely associated with erectile dysfunction. In this study, the researchers examined the association between nonsteroidal anti-inflammatory drug use and erectile dysfunction in a large, ethnically diverse cohort of men enrolled in the California Men’s Health Study.

Materials and Methods: This prospective cohort study enrolled male members of the Kaiser Permanente managed care plans who were 45 to 69 years old. Erectile dysfunction was assessed by a questionnaire. Nonsteroidal anti-inflammatory drug exposure was determined by automated pharmacy data and self-reported use.

Results: Of the 80,966 men in this study, 47.4% were considered nonsteroidal anti-inflammatory drug users based on the definitions used and 29.3% reported moderate or severe erectile dysfunction. Nonsteroidal anti-inflammatory drug use and erectile dysfunction strongly correlated with age with regular drug use increasing from 34.5% in men aged between 45 and 49 years to 54.7% in men aged between 60 and 69 years old with erectile dysfunction, increasing from 13% to 42%. The unadjusted odds ratio (OR) for the association of nonsteroidal anti-inflammatory drugs and erectile dysfunction was 2.40 (95% CI, 2.27, 2.53). With adjustment for age, race/ethnicity, smoking status, diabetes mellitus, hypertension, hyperlipidemia, peripheral vascular disease, coronary artery disease, and body mass index, a positive association persisted (adjusted OR 1.38). The association persisted when using a stricter definition of nonsteroidal anti-inflammatory drug exposure.

Conclusion: These data suggest that regular nonsteroidal anti-inflammatory drug use is associated with erectile dysfunction beyond what would be expected due to age and comorbidity.
Sanskrit name/Indian name: Haridra
English name: Turmeric

Introduction
The traditional spice and medicine turmeric is a low-growing perennial herb with lanceolate leaves and yellow flowers. Native to Southeastern Asia, turmeric is currently cultivated in India, China, Japan, Indonesia, Taiwan, Africa, Bangladesh, Sri Lanka, Burma (Myanmar), Thailand, Cambodia, Malaysia, and Philippines. India is by far the largest consumer, producer, and exporter of turmeric rhizome. In addition, India also exports turmeric preparations, essential oil, and oleoresin. Rhizomes are dried and ground into golden yellow powder used in cooking and medicine. They have a distinctive earthy fragrance.

History and Cultural Significance
The genus name Curcuma is the Latinized form of the Arabic al-kurkum, which originally meant saffron but now refers exclusively to turmeric. The common name, turmeric, comes from the French terra-mérite (Latin terra merita), meaning meritorious earth—probably because ground turmeric resembles the earth pigment ochre, and perhaps because of the regard in which turmeric was held by ancient people. In many languages, the name for turmeric means yellow root, and it is known as Indian saffron in many European languages, although it is a cheap and unacceptable substitute for true saffron (Crocus sativus). Known as the “golden spice” or the “spice of life,” turmeric has been held sacred and used medicinally in India for 4000 to 6000 years. During India’s Vedic period (ca. 1500–600 BCE), the orange-yellow rhizome of turmeric was called the “herb of the sun” and was regarded as the most outstanding healing herb.

Turmeric is widely used in the Indian systems of medicine (Ayurveda, Siddha, and Unani) as well as in Eastern Asian systems (Traditional Chinese Medicine [TCM], Japanese Kampo, Korean, and Malay). In the Ayurvedic system, depending on what it is combined with, main therapeutic uses of turmeric are in the treatment of disorders due to poison, ulcers, skin diseases and urticaria, urinary disorders, anemia, and chronic rhinitis/sinusitis. It is also used in Ayurveda for anorexia, cough, diabetic wounds, biliary and liver disorders, and rheumatism. Many Ayurvedic healers integrate the powder into a paste or lotion for the treatment of dry and flaking skin, skin sores and wounds, external inflammations, and painful arthritis. In the Unani system, turmeric is used therapeutically to treat ulcers, rheumatoid arthritis, conjunctivitis, eye strain, hiccough, asthma, catarrh, and itching.

Traditional medicinal practices in India and China tout the benefits of this bitter-tasting and slightly fragrant root as a digestive aid. In TCM, turmeric is specifically indicated for treatment of amenorrhea, mass formation in the abdomen, rheumatic pain of the shoulders and arms, traumatic swelling and pain, and pricking pain in the chest and abdominal regions. Turmeric is incorporated into teas and is a base component in many culinary spice blends, specifically curry. The fresh rhizome is preferred in Thailand, where it is grated and added to curry dishes and yellow curry paste. Yellow rice, made by the addition of fresh
or dried turmeric, is a dietary staple on the Eastern islands of Indonesia. Turmeric essential oil is used to improve the taste of stomach bitters, and the oleoresin is used in the food industry in sauces, soups, and instant meals.

Storing turmeric in its whole rhizome state is preferable as flavor and aroma dissipate quickly once the rhizome is powdered. However, powdered turmeric has an almost unlimited life as a dye.

In 1985, the German Commission E approved turmeric for the internal treatment of indigestion. The European Scientific Cooperative on Phytotherapy (ESCOP) recommends turmeric for mild digestive disturbances and minor biliary dysfunction. In 2008, the European Medicines Agency (EMEA) published a draft monograph, which once final, will be relevant for traditional herbal medicinal product (THMP) registrations in all EU Member States, including Germany. It proposes therapeutic indications for preparations of turmeric (eg, powdered rhizome, herbal tea, and 1:10 tincture with 70% ethanol) for the symptomatic relief of dyspepsia. Also in 2008, Health Canada published its final monograph for turmeric for the purpose of natural health product (NHP) compendial product license applications. Health Canada approved uses of the dried rhizome or preparations of the rhizome (eg, herbal tea infusion, 1:1 fluid extract and/or 1:5 tincture) as a carminative to help relieve flatulent dyspepsia and as a digestive aid. Official quality standards are available in the currently valid editions of the United States Pharmacopeia, British Pharmacopoeia, European Pharmacopoeia, Mexican Herbal Pharmacopoeia, Japanese Pharmacopoeia, Korean Herbal Pharmacopoeia, Pharmacopoeia of the People’s Republic of China, Ayurvedic Pharmacopoeia of India, Unani Pharmacopoeia of India, and others.

Based on centuries of use as a common spice and modern toxicological research, turmeric and curcumin are generally recognized as safe for use in foods and dietary supplements.

Turmeric has been suggested as a safe, natural, and effective alternative to now-recalled cyclooxygenase inhibitors such as celecoxib (Celebrex®) and rofecoxib (Vioxx®), as well as aspirin and ibuprofen.

**Modern Research**

Curcumin, a collective noun for a group of phenolic compounds called curcuminoids, is the most active chemical component in turmeric; it accounts for 2% to 5% of the spice and is responsible for the characteristic yellow color. Extensive in vitro and in vivo research over the past 50 years showed that curcumin may be helpful in several conditions and diseases. It possesses various properties such as antioxidant, anti-inflammatory, hepatoprotective, antimutagenic, anticarcinogenic, antitumor, antibacterial, fungistatic, and wound-healing properties.

Clinical studies show that curcuminoids may be beneficial in the prevention and treatment of various types of cancers, such as breast, colorectal, gastrointestinal, genitourinary, lung, leukemia, lymphoma, melanoma, ovarian, pancreatic, prostate, and sarcoma. In a clinical study, treatment with encapsulated turmeric resulted in the alleviation of peptic ulcers. A pilot study of 207 volunteers with irritable bowel syndrome (IBS) suggested that a standardized turmeric extract might help reduce IBS symptoms, although placebo-controlled trials were needed.

A short-term study investigating the antirheumatic activity of curcumin found that its effects were comparable with those of phenylbutazone, an analgesic and anti-inflammatory drug. Curcuminoids were also shown to produce a better anti-inflammatory response than placebo in postoperative inflammation in a small group of males who had hernia operations. A pilot study suggested that turmeric paste applied externally is an effective and inexpensive treatment for scabies, a condition caused by skin mites. Curcumin also shows beneficial effects on insulin resistance, a precursor of type 2 diabetes. Turmeric extract has shown some potential in prevention and treatment of neurodegenerative conditions, including Alzheimer disease. Other clinical trials suggest that curcumin might be helpful in treating familial adenomatous polyposis, ulcerative colitis, hypercholesteremia, atherosclerosis, pancreatitis, psoriasis, chronic anterior uveitis, and arthritis.

Also, turmeric is found to be effective in combination with other herbs. In one study, a combination of turmeric and Indian tinospora or guduchi (Tinospora cordifolia) was given to tubercular patients who were also receiving a treatment known to cause liver toxicity. That study found that the incidence and severity of hepatotoxicity was significantly lower in patients treated with the herb combination. Turmeric showed clinically significant results when studied in combination with Indian frankincense (Boswellia serrata) for osteoarthritis of the knee. Another clinical trial tested an eye drop preparation made from extracts of turmeric and seven other herbs from the Ayurvedic tradition on patients with a number of ophthalmic disorders. The herbal eye drop was successful in a variety of the
conditions and no adverse effects were observed. Research demonstrates that the oral bioavailability of curcumin is limited and is enhanced by combining it with piperine, a compound found in black pepper (Piper nigrum) and long pepper (P longum).

**Future Outlook**

In 2007, India accounted for over 71% of turmeric exports worldwide, followed by Vietnam (4.6%), China (2.7%), and Bangladesh (2.0%). India exported no more than 10% of its annual production of 527,980 tons in 2002–2003. As of 2007, India had 162,950 hectares (402,658 acres) of land for turmeric cultivation with a production of 552,300 tons. In the most recently reported 12-month export trade data (April 2007–March 2008), India exported 11,611.44 metric tons of fresh turmeric rhizome valued at US $8.23 million and 42,380.57 metric tons of dried and/or powdered rhizome, valued at US $33.95 million. During the same period, India also exported 355,930 kg of turmeric oleoresin, 54,660 kg turmeric preparations, and 1360 kg of turmeric essential oil.

Turmeric is susceptible to disease that can lead to a reduction in yield by as much as 80%. It is also susceptible to abruptly fluctuating prices due to changing trade relations and competing turmeric production in a number of countries. Since a sustainable turmeric economy is only possible when these risks are minimized, a number of policy measures are being considered in turmeric-producing countries, including healthy seed production, quarantine regulations to restrict transporting seed from one state to another when disease is a problem, and education of farmers regarding postharvest technology and the importance of keeping varieties separate since Alleppey and Madras turmeric are considered to be of higher quality than some others.


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**Aerobic Exercise as a Therapy Option for Migraine**

Exercise is assumed to have a positive effect on migraine. However, none of the studies on this topic can prove the expected positive influence of exercise. Therefore, the aim of this pilot study was to develop a training program suitable for migraine patients and to examine its effect on migraine. A total of 16 patients were examined; 8 migraine patients completed a 10-week aerobic running exercise program consisting of 3 workouts per week. The program was developed by sports scientists especially to increase the fitness level. Physical fitness (physical working capacity) was assessed using a PWC 150 test. There was also a control group of 8 patients without any special physical training. Migraine patients of the exercise group showed both a reduction in the number of migraine days per month \((P = .048)\) and the intensity of the attacks \((P = .028)\). An increase in fitness level resulted in a lowered stress level. Stress strategies like “displacement activity” \((r = −0.715; P = .046)\), “looking for self-affirmation” \((r = −0.742; P = .035)\), and “feelings of aggression” \((r = −0.802; P = .017)\) were reduced. Increasing the level of fitness (PWC 150) is one predictor for migraine improvement \((r = 0.409, P = .031)\). Aerobic exercise which leads to a better fitness level is an alternative therapy method for migraine.

Readers' Views

I take this opportunity to extend my sincere greetings, compliments, and good wishes for this excellent piece of work. The setup and the layout are enviably immaculate—the contributions make a stimulating reading. The Editorial is thought provoking. “Beliefs and Facts” and “Digressions” are entertaining, abstracts are plentiful, and advertisements are intelligently spaced. All told, it is a well-planned publication, and should find a place of pride to the doctor’s medical library. Congratulations!

VD Arora, Bombay, India
On the release of first issue of Probe

Hearty congratulations on the birth of Probe, an excellent journal in every respect. I am sure it will be highly appreciated by the medical profession. I have no doubt that the same high standard of editing, presentation, and printing will be maintained in the subsequent issues. It is bound to have a place of pride in the near future.

MP Vora, Bombay, India
On the release of first issue of Probe

“Excellent work! Keep it up!”
Dr S Senthil Kumar, Cuddalore, Tamil Nadu

“Excellent work”
Dr G Selvamooorthy, Dharmapuri, Tamil Nadu

“Nice communication”
Dr G Selvamooorthy, Dharmapuri, Tamil Nadu

“Excellent work”
Dr Prakash M Mirajkar, Satara, Maharashtra; Dr Bijaya Kumar Meher, Orissa; Dr Ankur L Raval, Anand, Gujarat

“All articles are best and appropriate”
Dr AC Srivastava, Gorakhpur, Uttar Pradesh

“Good images/pictures”
Dr Amit Subhash Dixit, Satara, Maharashtra

You must have received many congratulatory letters on your excellent anniversary number, but perhaps only a few of them must have taken note on your editorial claim that, you have the satisfaction to find the Probe attaining a place of distinction so soon in the annals of Indian medical journalism. As one who frequently scans a number of medical journals from here and abroad, permit me to state that the Probe despite its commercial affiliation, has scored a new high in the sphere of medical journalism. The task might be difficult, but as a reader-addict of your bimonthly, I confidently feel, that it will be done to every satisfaction.

Here wishing the Probe, many successful happy returns.

KB Desai, Bombay, India
On the release of first anniversary issue of Probe
Extracted from: Probe. 1962;II(2):77.

“I have been going through the contents of your journal with much interest and no little profit. I would like to congratulate you on your successful efforts in bringing out this very excellent periodical, which definitely has a significant role in progressive and up-to-date medical press of Bombay.

Jelal M Shah, Karachi, Pakistan
Extracted from: Probe. 1962;II(2):77.

“Thanks for the articles and information; these are very useful for Ayurvedic medicine doctors”
Dr Thakur Prasad Sahu, Daman and Diu

“Probe is unique. I wish a good future for Probe and The Himalaya Drug Company”
Dr Shiva Kumar, Kolar, Karnataka

“Please send Probe regularly to improve our clinical knowledge”
Dr ND Jagannatha, KR Nagar, Mysore, Karnataka

“Probe is very informative. Please try to publish it monthly”
Dr RK Dwivedi, Allahabad, Uttar Pradesh

“I am very very satisfied with Probe and its content”
R Kishor Patil, Dombivli, Maharashtra

“Probe is very informative”
Dr AB Samanta, Burdwan, West Bengal

“Probe is very helpful in clinical practice”
Dr Manoranjan, Puri, Orissa

“Contents of Probe are very informative”
Dr Smeeta Kamat, Goa

“Probe as a presentation of The Himalaya Drug Company is as big and great as the Himalayas”
Dr JS Sharma, Amaravati, Andhra Pradesh

“Overall appeal is excellent”
Dr GP Sharma, Alwar, Rajasthan

Dr Amit Majumdar
(address not available)

R Kishor Patil, Dombivli, Maharashtra

Dr AB Samanta, Burdwan, West Bengal

Dr Amrit Majumdar (address not available)

“Good picturization along with disease explanation”
Dr (Mrs) Raju Sharma, Ludhiana, Punjab

“Herbal Notes is an excellent feature! Have more of it!”
Dr AB Samanta, Burdwan, West Bengal

“The information provided in Probe is valuable and excellent to know and treat diseases”
Dr Prakash D Barki, Hubli, Karnataka

“Probe magazine is very good and best as study material”
Dr MT Mohite, Amala, Maharashtra

“Continue the good work. Best of luck”
Dr HS Chawla, New Delhi
“I think Probe is a complete magazine for doctors and medical students”
Dr Nitin Ujjaliya, Ujjain, Madhya Pradesh; Dr GC Patel, Mehsana, Gujarat; Dr Vinod Dwivedi, Jabalpur, Madhya Pradesh; and Dr Doulasab I, Raichur, Karnataka

“Very good and informative magazine for Ayurvedic doctors”
Dr BP Tamrakar, Bhilai, Chhattisgarh

“Good publication for Ayurvedic students, interns, and doctors”
Dr BP Tamrakar, Bhilai, Chhattisgarh

“Keep it up”
Dr Ravi Sankar Reddy, Piler, Andhra Pradesh

“Nice piece of work”
Dr Mohan Goldsmith, Bidar, Karnataka

“Overall, all the topics/sections of Probe are good”
Dr Ramesh, Vishakhapatnam, Andhra Pradesh

“Kindly send me other publications/literatures published by you”
Dr Hemant Laxman Vinze, Mumbai

“Nice work”
Dr Gorwade Sanjeev Kumar, Bidar, Karnataka

“Probe is an extremely powerful and useful magazine…cannot describe its quality in words”
Dr JS Chauhan, Meerut, Uttar Pradesh

“Keep probe up”
Dr SK Saifi, GB Nagar, Uttar Pradesh

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Dr MH Shivanand, Bellary, Karnataka; Dr Rakesh Joshi, Udaipur

“The look of Probe is very good and matches international standards. Keep it up”
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“Probe is an extremely useful for our profession”
G Durga Mahesh, Vizianagaram, Andhra Pradesh

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Dr S Gowri Sankar, Dharmsar, Andhra Pradesh

“Very good”
Dr Ashok R Soni, BSAM, Ahmedabad, Gujarat

“Please make Probe online also, so that more number of doctors can read it”
Dr Nikul B Patel, Ahmedabad, Gujarat

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Dr Nikul B Patel, Ahmedabad, Gujarat
Himalaya Baby Care Products

Himalaya’s inception can be traced back to the year 1930 when Mr. M. Manal, founder of The Himalaya Drug Company, decided to present Ayurveda to the world in a contemporary form and unravel the mystery behind the 5000-year-old system of medicine. As a result, products of Himalaya are rooted in Ayurveda and backed by years of research—a true synergy of thousands of years of herbal wisdom and modern scientific research. Eight decades later, we have our presence in 67 countries with a range of over 200 products spanning pharmaceutical, personal care, baby care, and animal health. It covers the entire wellness spectrum, offering head-to-heel herbal health care catering to all kinds of people and their different needs.

Liv.52, a liver protective, and Bonnisan, a health tonic for infants and children, are classic examples of innovative research of Himalaya. These products have become a vital part of the family’s health regimen. Bonnisan, for instance, is widely trusted by doctors, pediatricians and mothers, for its safety and efficacy.

With a legacy of research expertise in herbal medicine, including therapeutic products for child health, the next step for Himalaya was “naturally” a range of herbal baby care products.

A comprehensive portfolio that suits every need of your baby, the Himalaya baby care range includes clinically proven pharmaceutical-grade herbal products based on Ayurvedic formulations. Therapeutic herbs such as khus-khus, Indian madder, licorice, and olive have been used in these products to provide gentle care to your baby. Each product, clinically tested by pediatricians in leading hospitals, has 100% herbal actives specially blended to make it safe, effective, mild, and soothing.

The uniqueness of the range lies in understanding the needs of babies and combining it with Ayurveda’s philosophy of child care. Known as “Kaumarabhritya” or complete care for the child, the philosophy encompasses nursing, nourishing, and supporting the needs of the child to grow into a happy and healthy adult.
Celebrating 50+ years of
Liv.52

Then

Preliminary Observation on the Role of Liv.52 in Infective Hepatitis with Persistent Jaundice

Rath BB, et al.

*Capsule*. 1975;XV(8):170-175.

This study was conducted to examine the effect of Liv.52 in patients with infective hepatitis and persistent jaundice. A total of 15 patients with infective hepatitis and jaundice (persistent for more than 6 weeks) were included in the study. These patients received Liv.52 at a dosage of 2 tablets, three times a day. They were examined every week during the treatment period for degree of jaundice, liver size, general feeling, and appetite. At the end of 8 weeks, bromosulphalein (BSP) excretion test and liver biopsy were performed and results were evaluated. The results showed that jaundice disappeared at the end of 8 weeks in all patients, except for one. Serum bilirubin levels and BSP excretion were normalized. All patients experienced a feeling of general well-being and improvement in appetite. These findings suggest that Liv.52 is beneficial in infective hepatitis with persistent jaundice.

Now

Meta-analysis to Evaluate the Efficacy and Safety of Liv.52 in Infective Hepatitis

Kolhapure SA, et al.


A meta-analysis of 50 clinical studies (three double-blind placebo-controlled; 21 placebo-controlled; 22 noncomparative; and four case studies) conducted over a span of 30 years was performed to evaluate the safety and efficacy of Liv.52 in infective hepatitis. The mean duration of these studies was 6.62 months. Each study was abstracted for the number and ages of enrolled patients, changes in the biochemical parameters (serum bilirubin [SB], serum glutamic oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], serum alkaline phosphatase [SAP], serum albumin [SA] and serum globulin [SG], and prothrombin time [PT]) from baseline to values at the end of study. Cumulative data analysis showed a significant reduction in the mean SB, SGOT, SGPT, AP levels, PT, and mean period required for total (symptomatic, clinical, and biochemical) recovery. The decreased SA and SG levels were also increased significantly, when compared to the pretreatment values, in all studies. There were no reported or observed significant adverse events in all trials. Therefore, this meta-analysis concludes that Liv.52 tablets and syrup are safe and effective in the management of infective hepatitis.

I have been prescribing Liv.52 to majority of patients who are kept on anti-TB therapy as it prevents jaundice and rise of hepatic enzyme, which are found to be elevated in these patients. As the presence of nausea, vomiting at times makes patient defaulter, Liv.52 helps the patient from becoming a defaulter from therapy. The clinical study conducted by me in coma and pre-coma patients of viral hepatitis was published in Probe (1974). Liv.52 was found to be very efficacious and prevented mortality in majority of patients. I have been prescribing Liv.52, Septilin, and Abana. I have found encouraging results with all the products.

Dr SH Talib
Professor & Head, Department of Medicine, Maharashtra Gandhi Mission’s Medical College & Hospital Aurangabad 431001
Maharashtra
Cystone

Then

Oral Treatment for Urolithiasis

Benker YG.

*Med Digest.* 1954;August:441.

This study was conducted to evaluate the role of oral therapy (Cystone) in urolithiasis.

The study evaluated a total of 14 patients with urinary complaints: six cases with renal calculi, two with vesical calculi, and four with crystalluria and/or renal colic.

Diagnosis was confirmed by urine and x-ray examinations. All patients were administered Cystone at a dosage of 2 tablets three times a day for 2 months.

At the end of the study, all patients experienced complete symptomatic relief.

Now

Safety and Efficacy of Cystone in the Management of Ureteric Calculi

Mohanty NK, et al.


A prospective, randomized, double-blind, placebo-controlled study was conducted to evaluate the safety and efficacy of Cystone tablet in reduction/expulsion of ureteric calculi and providing relief from clinical symptoms associated with urolithiasis. The study included 52 patients with upper urinary tract calculi (5–10 mm diameter). These patients were randomized to receive either Cystone or placebo at a dosage of 1 tablet, three times a day, for 6 months. Urine microscopy results; hematological parameters; and symptoms such as severity of pain, number of pain episodes, fever, low backache, and decrease in frequency of urination were evaluated.

The results of the study showed that in patients treated with Cystone, there was a significant reduction in the size of the calculi; severity of abdominal pain; microscopic hematuria, pus cells (pyuria), bacteriuria, and crystalline sediments; and size of the stone. A considerable reduction in the size of the calculi and relief from the symptoms (with improvement in urine parameters), were also noticed in these patients. These findings suggest that Cystone tablet is safe and effective in the management of urolithiasis.

I have experienced good results from Cystone in the prevention and management of small renal stones (3–5 mm). Owing to its diuretic, mucin-dissolving, and antibacterial activities, majority of the stones disappeared with long-term administration of Cystone. I have not come across any significant adverse reactions with Cystone, and thereby can be liberally recommended for the treatment of small renal calculi.

Dr T Narender

Consultant Urologist and Andrologist, Emergency and Critical Care, Abhaya Hospitals, Khammam, Andhra Pradesh

Launched in 1943
Pilex

Then

Indigenous Therapy for Piles

Varandani BP, et al.

The Ind Pract. 1969;XXII(9):545-547.

The present study was conducted to evaluate the efficacy of Pilex in the treatment of piles (hemorrhoids). A total of 70 patients with hemorrhoids were included in the study. These patients received Pilex tablets at a dosage of 2 tablets three times a day for 1 to 2 months. They were instructed to use Pilex ointment locally. The results of the study showed that 60 patients were relieved of their symptoms after 10 days of treatment initiation, although the therapy was continued for 1 month. In 10% of the cases, the therapy had to be continued for 2 months. The overall response rate was 87.1% (40 patients experienced complete relief and 21 patients had partial relief).

Now

Clinical Evaluation of PIL-28 (Pilex) in the Management of Hemorrhoids

Vastrad CS, Pakkanavar RV.

Antiseptic. 2002;99(9):343-344.

The present study was conducted to evaluate the safety and efficacy of PIL-28, a formulation containing herbs and minerals for the management of hemorrhoids, in 50 patients of either sex, aged between 22 and 63 years. Among the patients, 31 had external hemorrhoids, 10 had internal hemorrhoids, and 9 had both internal and external hemorrhoids. Patients were given PIL-28 at a dosage of 1 tablet twice daily for 6 weeks. At the end of 6 weeks, patients were evaluated for the efficacy and tolerability of PIL-28 tablets. Results of the study revealed that response to PIL-28 was very good in 56.25% of patients and good in 37.50% of the patients, showing a significant improvement in general health and a gross reduction of associated symptoms. There were no side effects observed during the treatment and follow-up period.

Pilex tablets and Pilex ointment combinational therapy is very effective in all types of hemorrhoids. Pilex is one of the best indigenous drugs available in the market. I have been using this drug in my practice form the past 30 years.

Dr Nair GR
Formerly Senior Medical Officer
(to Govt. of Kerala)
Flat no. 3B, Alliance tower, Minchin road, Thycad post, Thiruvanathapuram – 695014
Septilin

Then

Treatment of Upper Respiratory Infections with Septilin
Gokhale SG, Wakharia PV


The present study was conducted to evaluate the role of Septilin in the treatment of upper respiratory tract infections. The study included a total of 75 patients who received Septilin at a dosage of 2 tablets three or four times a day for a period of 2 to 4 days. The results of the study showed that Septilin was useful in about 75% of the cases and nasal discharge stopped in 48 hours. There was a significant and quick improvement in symptoms such as sneezing, watery nasal discharge, headache, pain and dryness in the throat, sore throat, cold, malaise, stuffiness in nose, body ache, cough, and fever. Therefore, it can be concluded that Septilin has a place in the treatment of mild upper respiratory infections particularly in common cold, allergic rhinitis, and pharyngitis.

Now

Clinical Efficacy and Safety of Septilin Tablets in Respiratory Tract Infections: A Meta-analysis

Kshirsagar M, et al.


The aim of this study was to perform meta-analysis on the efficacy and short- and long-term safety of Septilin tablet in respiratory tract infections (RTIs), as reported in 38 published studies conducted between 1958 and 2001 in 2765 patients with RTI. Adult patients received 1 to 2 tablets, TID for 7 days to 3 months and children were administered one-quarter tablets QID to 1 tablet TID for 7 days to 3 months. Improvement in symptoms, clinical recovery, and immunoglobulin levels were evaluated. Results showed statistically significant improvement in patients with RTI. Of the 1613 patients with upper respiratory tract infection (URTI), 1211 patients responded to the Septilin therapy and among the 838 patients with lower respiratory tract infection (LRTI), 720 patients responded to the therapy. In comparative control trials, 74.42% of patients treated with Septilin improved as compared to 52.86% of patients treated with antiallergics and antibiotics. Immunoglobulin (IgG, IgA, and IgM) levels showed significant improvement with Septilin. Therefore, it can be concluded that Septilin tablets are safe and effective in treating RTIs.

This is to certify that I have used Septilin in ENT cases with chronic disorder and found good results. I would recommend Septilin tablets in chronic ENT conditions to prevent recurrence.

Thanking you
Dr Rupa S Thakur
ENT Specialist
Clinic: Trinuriti Arcade, Near Sarvodaya hospital, LBS Marg, Ghatkopar, Mumbai

Launched in 1956
The present study was conducted to evaluate the efficacy of Gasex in common gastrointestinal complaints. A total of 50 patients with various gastrointestinal symptoms such as abdominal discomfort, heartburn, acid regurgitation, nausea and vomiting, gaseous distension of abdomen, belching, flatulence, and feeling of fullness in epigastrium were included in this study. Each patient received Gasex at a dosage of 3 tablets, three times a day, for 2 to 3 weeks and the effect of the drug on symptomatic relief was assessed. The results of the study showed a considerable improvement in the signs and symptoms. More than 70% of the patients experienced complete relief. The results were excellent in 29 patients, good in 13, and fair in 8. No adverse effects were observed during the study. These observations prove the definite usefulness of Gasex tablets in common gastrointestinal complaints.

This meta-analysis was conducted to evaluate the efficacy and short- and long-term safety of Gasex tablets in gastrointestinal disorders and in preradiographic preparation of patients, as reported in 17 published study reports conducted between 1971 and 1997. These studies were conducted in 790 patients with gastrointestinal disorders or 2910 patients who were sent for preradiographic preparation. Patients with gastrointestinal disorders were administered 2 tablets three times a day for a period of 3 days to 8 weeks, whereas patients sent for preradiographic preparation were administered 2 tablets three times a day or 4 tablets four times a day for a period of 3 days prior to the radiography procedure. Relief from gastrointestinal symptoms and gas-free radiographic findings were taken into consideration. Results of the study showed that patients treated with Gasex tablets had statistically significant relief from gastrointestinal disorders and they also ensured better radiological interpretation in patients sent for preradiographic preparation. No adverse effects were either reported or observed during any of the studies.

I have been prescribing Gasex tablets to my patients from past 20 years and getting good results for symptoms such as flatulence and belching. I prescribe Gasex along with Herbolax capsule for patients before undergoing abdominal radiology and getting good results. Of late, I have started recommending Gasex syrup too.

Dr Manorama Agarwal
Consultant Physician and Gynecologist
1/4, paper mill colony, Nishatganj, Lucknow
**Tentex forte**

**Then**

Clinical Trials with Tentex Forte in Functional Impotency

Sahu KC


The present study was conducted to evaluate the efficacy and safety of Tentex forte in functional impotency. A total of 26 patients (aged between 22 and 55 years) experiencing impotency and 10 normal individuals/five couples (control) were included in the study. These patients received 2 tablets daily for a period of 1 week. The dosage was customized accordingly in patients addicted to alcohol. The results of the study showed that Tentex forte brought about remarkable improvement in functional impotency and sexual neurasthenia, in both the younger and elderly age groups, although the elderly age group required a higher dosage and longer treatment. In case of alcoholic addicts, gratifying results were noticed a little later in the third or fourth week. Tentex forte improved sexual desire and prolonged the duration in controls.

**Now**

Clinical Evaluation of Tentex forte and Himcolin cream in the Treatment of Functional Erectile Dysfunction

Bostandjiev R, Mitra SK.


This open clinical trial was conducted to determine the efficacy of Tentex forte and Himcolin cream, used concurrently in men with functional erectile dysfunction. A total of 50 men aged between 19 and 59 years were included in the trial. These patients were administered Tentex forte at a dose of 2 tablets, twice daily, combined with local application of Himcolin cream on the penis and pubic area before sexual intercourse. The different aspects of erection and sexual functioning were evaluated before treatment and after 2 and 4 weeks of treatment. The results of the study showed that there was a rapid improvement in the ability to penetrate and maintain erection after 2 weeks of treatment with Tentex forte and Himcolin cream. The results were statistically significant after the fourth week of therapy (*P*<.001). The findings also documented that therapy with Tentex forte and Himcolin cream improves the quality, frequency, and sustainability of erection, sexual desire, orgasmic response, and overall satisfaction.

I have recommended Tentex forte tablets to more than 1 lakh patients in the past 25 years. I prescribe Tentex forte at a dosage of 2 tablets BID for improving libido, and maintaining penile erection. It acts as a complete Kayakalp, aphrodisiac, and stimulant and helps in rejuvenating the genitourinary tract. Tentex forte is ten times more potent when compared to other medications.

Dr Shaikh AH

Navjeevan Ayurvedic Dispensary

Near Central Bus Stand, Opposite Siddharth Garden, Behind Kamgar Kalyan Kendra,

Aurangabad – 431001, Maharashtra
**Lukol**

**Then**

Lukol in the Treatment of Leucorrhea

Bhagwat SS.  

The present study was conducted to evaluate the effect of Lukol in the treatment of leucorrhea. A total of 25 patients were considered for the study and were divided into three groups according to the character of discharge, associated cervical erosion, etc. Group I (n = 4) had excessive normal discharge; group II (n = 11) had nonspecific vaginitis with erosion and endocervicitis; and group III (n = 5) had specific vaginitis including trichomoniasis and moniliasis. These patients were treated with Lukol tablets for a minimum period of 3 weeks and followed up for 2 to 4 months after the cessation of therapy to note if any relapses occurred. The results of the study showed that in all cases, the associated symptoms including malaise, poor appetite, and constipation were alleviated and the patients experienced a general sense of well-being. From these findings, it can be concluded that Lukol is a promising drug in the oral therapy of leucorrhea.

**Now**

A Study of Lukol in Leucorrhea, Pelvic Inflammatory Diseases, and Dysfunctional Uterine Bleeding

Tewari PV, et al.  

This clinical study was conducted to evaluate the efficacy of Lukol in leucorrhea, dysfunctional uterine bleeding (DUB), and symptoms of pelvic inflammatory disease. A total of 60 women with leucorrhea, DUB from puberty to premenopause, or with symptoms of pelvic inflammatory disease were included in the study. Vaginal discharge with pain and itching in vulva and vagina and painful coitus were the chief complaints among patients with leucorrhea while vaginal discharge, pain in lower abdomen, backache, pain during menstruation, and irregular menstruation were the common complaints of PID cases. Women with DUB were suffering from excessive bleeding, early periods, weakness, and palpitation. All the patients received Lukol tablet at a dose of 2 tablets, three times daily for 15 days. The duration of treatment was in accordance to the relief in symptoms; however, DUB cases were advised to take the medication for three consecutive months. All the cases were followed fortnightly for a period of 6 months. The results showed significant improvement in symptoms in all the three groups. Patients with leucorrhea reported improvement within 7 to 10 days after treatment and complete recovery within 1-month period and complete relief from PID and DUB was reported after 45 days and 3 months, respectively.

I am prescribing Lukol for the past 9 to 10 years and found it to be very effective in nonspecific leukorrhea, leukorrhea post IUCD and tubectomy, and leukorrhea associated with pelvic inflammatory disease. Lukol shows maximum benefits after 3 months of treatment.

**Dr Usha Sharma**  
Consultant Obstetrician and Gynecological Surgeon  
Obs & Gyne Surgical Clinic, Patna

Year of Launch: 1955
Liv.52® HB (CAPSULE)

Effective management of Hepatitis B

Liv.52 HB, a US patent-pending phytopharmaceutical formulation, is recommended for the treatment of hepatitis B. Liv.52 HB protects the liver against various hepatotoxins, exerts antiviral activity, and enhances antioxidant defense system. Liv.52 HB is safe even for long-term administration.

**Composition**
Each Liv.52 HB capsule contains:

- Exts.
- Mustaka (Cyperus rotundus) 125 mg
- Nagaramustaka (Cyperus scariosus) 125 mg

**Clinical Pharmacology**
Liv.52 HB has antiviral, hepatoprotective, anti-inflammatory, immunomodulatory, and antioxidant actions.

Liv.52 HB suppresses the replication of viral DNA involved in hepatitis B and eliminates the hepatitis B virus (HBV) by reverse transcriptase inhibition. Liv.52 HB suppresses HBV by binding to the surface antigen HBsAg. Liv.52 HB prevents the loss of functional integrity of the hepatic cell membrane, ensures early restoration of hepatic functions in infective hepatitis due to its antiperoxidative activity. Liv.52 HB capsule protects the hepatic parenchyma and promotes hepatocellular regeneration.

**Indication**
Hepatitis B infection

**Dosage**
1 to 2 capsules twice daily after meals.

**Route of Administration**
Oral.

**Side Effects**
Not reported.

**Adverse Reactions**
Not reported.

**Drug Interactions**
No clinically significant drug interactions have been reported to date.

**Warnings**
None

**Precautions**
None

**Contraindications**
No absolute contraindications.

**Presentation**
Box of 3 blister-pack of 10 capsules each.

**Pharmacological Actions of Principal Ingredients**

**Antiviral action**
Premashis Kar et al observed in their clinical trial that oral administration of the extracts *C. rotundus* and *C. scariosus* resulted in significantly lowering of the viral load in almost all the patients after 24 weeks of treatment. Herbal extract containing *C. rotundus* and *C. scariosus* showed surface antigen (HbsAg) suppression and HBV virus elimination. The formulation containing extracts of *C. rotundus* and *C. scariosus* demonstrated HBV elimination by way of reverse transcriptase inhibition.

**Hepatoprotective action**
A clinical trial showed that administration of a formulation containing extracts of *C. rotundus* and *C. scariosus* exerted hepatoprotective effect by reversing the oxidative damage by hepatocytes. Pretreatment
with the extract of *C. scariosus* significantly lowered (*P<0.05*) the serum ALP, GOT, and GPT levels and significantly prevents (*P<0.05*) CCl4-induced rise in serum liver enzymes.

**Renormalization of liver functions**

Six months of therapy with the formulation containing the extracts of *C. rotundus* and *C. scariosus* was markedly effective in the majority of patients as it resulted in disappearance or alleviation of abdominal pain and poor appetite. Treatment with the extracts of *C. rotundus* and *C. scariosus* showed improvement in appetite and reduction in jaundice.

**Anti-inflammatory action**

In vivo studies have demonstrated the anti-inflammatory potential of extract of *C. rotundus* in acute models of inflammation such as carrageenan-induced rat paw edema and acetic acid-induced peritonitis in mice.

**Immunomodulatory action**

Treatment with formulation containing extracts of *C. rotundus* and *C. scariosus* showed immunomodulatory effects by causing the release of nitric oxide (NO) by macrophages and cytokines like TNF-α.

**Antioxidant action**

Studies on rats showed that the extracts containing *C. rotundus* and *C. scariosus* caused inhibition of lipid peroxidation and enhancement in the activity of antioxidant enzymes due to the direct free radical-scavenging activity and reactivation of these enzymes in the liver.
Clarina® ANTI-ACNE KIT

Clarina anti-acne kit contains one tube each of: Clarina anti-acne face wash gel, Clarina anti-acne face mask, and Clarina anti-acne cream. This Clarina anti-acne kit offers a polyherbal anti-acne regimen, recommended for comprehensive management of acne.

Clarina® ANTI-ACNE

FACE WASH GEL
Clarina anti-acne face wash gel is a polyherbal formulation recommended for daily cleansing of face afflicted with acne.

Composition
Each gram of Clarina anti-acne face wash gel contains:

- Extracts: Kumari (Aloe barbadensis) 1.0 mg, Nimba (Azadirachta indica) 0.5 mg, Haridra (Curcuma longa) 0.5 mg, Jalavetasa (Salix tetrasperma) 0.1 mg.
- Other ingredients: Phenoxyethanol, Methylchloroisothiazolinone, Methylisothiazolinone, Sodium Benzoate, Potassium Sorbate.

Pharmacology
Clarina anti-acne face wash gel has cleansing activity that gently cleans the skin and leaves it feeling fresh and soft all the day. It has antibacterial, anti-inflammatory, antioxidant, astringent, and soothing effects, which help synergistically in the management and prevention of acne. Clarina anti-acne face wash gel is suitable and safe to use on oily/greasy type of skin.

Indication
Acne vulgaris

Directions for Use
Moisten face, apply required quantity of the gel and gently work up lather with a circular motion. Wash off and pat dry. Recommended twice daily.

Route of Administration
Topical

Side Effects
Not reported.

Adverse Effects
Not reported.

Drug Interactions
No clinically significant drug interactions have been reported.

Special Warnings
None

Precautions
It is advisable to apply a small amount of Clarina anti-acne face wash gel on the skin behind the ear lobe to confirm safety of topical application in individuals with diathesis of allergy. If any allergic or hypersensitivity reaction occurs, Clarina anti-acne face wash gel should not be used. If a hypersensitivity reaction occurs, wash the face immediately and keep it dry. Severe reaction may require conventional treatment.

Contraindications
No contraindications.

Presentation
60 mL tube

Storage
Store in a cool and dry place, away from direct sunlight. Do not refrigerate. Keep out of the reach of children.

Clarina® ANTI-ACNE

FACE MASK
Clarina anti-acne face mask is a polyherbal formulation recommended for deep cleansing of pores in management of acne.

Composition
Each gram of Clarina anti-acne face mask contains:

- Extracts: Haridra (Curcuma longa) 1.0 mg, Kumari (Aloe barbadensis) 0.5 mg, Jalavetasa (Salix tetrasperma) 0.1 mg.
- Other ingredients: Methylchloroisothiazolinone, Methylisothiazolinone, Sodium Benzoate, Methylparaben, Propylparaben, Phenoxyethanol, Ponceau SX.

Pharmacology
Clarina anti-acne face mask deep cleanses and soothes the skin. Its
antiseptic, astringent, and wound-healing activities have a synergistic effect in management of acne. Its additional sun-protection activity protects the skin from harmful UV rays and prevents skin irritation. Clarina anti-acne face mask does not contain any bleach. It is dermatologically tested and suitable for all skin types.

**Indication**

Acne vulgaris

**Directions for use**

Apply evenly over cleansed face and neck, avoiding the area around eyes. Allow it to dry for 10 to 15 minutes. Remove with wet sponge and wash the skin with cool water. Recommended once or twice a week.

**Route of Administration**

Topical

**Side Effects**

Not reported.

**Adverse Effects**

Not reported.

**Drug Interactions**

No clinically significant drug interactions have been reported.

**Special Warnings**

None

**Precautions**

It is advisable to apply a small amount of Clarina anti-acne face mask on the skin behind the ear lobe to confirm safety of topical application in individuals with diathesis of allergy. If any allergic or hypersensitivity reaction occurs, Clarina anti-acne face mask should not be used.

If a hypersensitivity reaction occurs, wash the face immediately and keep it dry. Severe reaction may require conventional treatment.

**Contraindications**

No absolute contraindications.

**Presentation**

75 mL tube

**Storage**

Store in a cool and dry place, away from direct sunlight.

Do not refrigerate. Keep out of the reach of children.

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*Clarina® ANTI-ACNE CREAM*

**Description**

Clarina anti-acne cream is a natural formulation recommended for all-day and all-night protection against acne.

**Composition**

Each gram of Clarina anti-acne cream contains:

- **Extracts:** Kumari (*Aloe barbadensis*) 200 mg, Badama (*Prunus amygdalus*) 10 mg, Matsyakshi (*Alternanthera sessilis*) 10 mg, Manjishtha (*Rubia cordifolia*) 5 mg.

- **Powders:** Tankana 12.5 mg, Yashad bhasma 12.5 mg, Base q.s. ad 750 mg.

- **Other ingredients:** Methylparaben IP, Propylparaben IP, Bronopol IP.

**Pharmacology**

Acne vulgaris is a steatorrhoeic chronic disease, which is manifested as blackheads, papulo pustular eruptions, purulent cysts, and cicatrices. Recent evidence shows that *Propionibacterium acnes* and peroxisome proliferator activated receptors (whose natural ligands are PUFA and their oxidation products) are important links between oxidative damage and acne vulgaris. Clarina anti-acne cream has antibacterial, anti-inflammatory, wound-healing, astringent, and soothing effects, which act synergistically in the management of acne.

**Indication**

Acne vulgaris

**Directions for use**

Wash the face with Clarina anti-acne face wash gel and apply Clarina anti-acne cream twice daily on acne lesions and inflamed surfaces until the lesions heal completely.

**Route of Administration**

Topical

**Side Effects**

Not reported.

**Adverse Effects**

Not reported.

**Drug Interactions**

No clinically significant drug interactions have been reported.

**Special Warnings**

None

**Precautions**

It is advisable to apply a small amount of Clarina anti-acne cream on the skin behind the ear lobe to confirm safety of topical application in individuals with diathesis of allergy. If any allergic or hypersensitivity reaction occurs, Clarina anti-acne cream should not be used.

If a hypersensitivity reaction occurs, wash the face immediately and keep it dry. Severe reaction may require conventional treatment.

**Contraindications**

No absolute contraindications.

**Presentation**

30 g tube

**Storage**

Store in a cool and dry place, away from direct sunlight.

Do not refrigerate. Keep out of the reach of children.
Herbal Apps for iPhone® and iPod Touch®

These days there seems to be an iPhone® and iPod Touch® application, or “app,” for just about everything—and herbal information is no exception. More than 100 herb-related apps are now available to consumers, including Herbs+, Herb Garden, Herbs & Spices, iPlant, Natural Cures, and Qpalm Herb.

Jacob Teitelbaum, medical director of the National Fibromyalgia and Fatigue Centers, began the free Natural Cures iPhone app in November 2008. He co-wrote the app’s content with his wife Laurie Teitelbaum, a nutritionist, Nambudripad’s Allergy Elimination Techniques (NAET) practitioner, and—as he described her—an “avid iPhoner.”

“It was my wife’s idea,” said Dr Teitelbaum. “The goal is to make straightforward information available to the public in easy-to-understand language, and documented in the scientific literature. We accept no advertising and no money from pharmaceutical companies or natural product companies, to keep the information objective and very credible. We decided to make it free, as part of our goal of empowering the public with information.”

As of January 2010, the app had been downloaded by approximately 750,000 people, according to Dr Teitelbaum, and Natural Cures is regularly ranked among the top 25 free apps within the Health and Fitness category—often in the top 10.

The app notes herbal, nutritional, lifestyle, and other treatments for common health conditions, mainly found under an A–Z listing of those conditions. Some of the herbal recommendations include passionflower (Passiflora incarnata) and magnolia (Magnolia officinalis) for anxiety; licorice (Glycyrrhiza glabra) for adrenal exhaustion; and willow (Salix alba), frankincense (Boswellia serrata), and cherry (Prunus avium) for arthritis. Natural Cures information is available free online at www.vitality101.com for those without an iPhone or iPod Touch.

Jeff Lundgren of Lundgren Consulting LLC., who specializes in software and Internet development, has had a personal interest in the outdoors and survivalist techniques for many years. This led him to develop iPlant, a $1.99 app that includes information on more than 300 commonly used herbs and plants, including their Latin and common names, history, culinary uses, medicinal properties and uses, and safety warnings.

The information found in iPlant has been collected from a variety of sources, including content provided personally from Lundgren’s research.

According to Lundgren, iPlant has been downloaded thousands of times in the last year since its release for the iPhone and iPod Touch. Based on feedback, he believes that the app is primarily popular among laypersons and plant enthusiasts, not necessarily plant professionals.

The $2.99 Herbs & Spices app was created by software developer Ganesh Thambiran at BuzzLifeApps. With a degree in biology and a high interest in botany, Thambiran features 66 commonly used herbs and spices in his app, with each entry including such information as Latin and common names, health benefits, history, and traditional uses. The app mainly focuses on culinary herbs and is available in the following languages (in addition to English): Chinese, Japanese, Spanish, Russian, Italian, and German.

Each listing appears beside a plant icon of the specific plant, while each individual entry includes a larger plant picture for easy identification. According to Thambiran, he took many of the herbal photos himself, while also outsourcing a few to photographers.

More information about this app is available at www.buzzlifeapps.com.

When choosing an herbal app, a useful resource is PC World’s App Guide (www.pcworld.com), which includes reviews about technological products, software, and downloads. Over 100 apps match the search criteria “herbs.” The iTunes App store also offers valuable information, including user ratings and reviews.

World over, there is a growing awareness and concern for health and a strong shift from curative advised healthcare to preventive healthcare. To tune in to the trend early on, The Himalaya Drug Company, in March 2002, launched Pure Herbs, a range of individual herb extracts like Tulasi, Neem, and Brahmi.

The Himalaya Pure Herbs brand is a range of specially selected individual herbs that can be used individually to treat/manage specific ailments and maintain wellness of the body. Himalaya Pure Herbs has the pure and concentrated goodness of herbs in the right measure that are scientifically tested and guaranteed for the highest quality and potency.

Benefits of Herbs

Herbs have been used, both as food and medicine, for centuries to eliminate excesses and minimize deficiencies in body. The value of using herbs lies particularly in their mildness to the body. While herbs may provide nutrition to the body, their primary function is to stimulate or improve body functions. Recent research has helped prove and define the pharmacological activities of individual herbs.

Why Pure Herbs?

The herbs that feature in the Pure Herbs range have remarkable benefits and are proven for their authenticity, quality and efficacy. Everyone can benefit from the goodness of these herbs, irrespective of sex, body type, or state of health and metabolic functions. Pure Herbs, the pure and concentrated strength of a single herb in the right measure, stimulate and improve body functions. Each Pure Herb is a potent extract and a treasure of active constituents that work by synergistic activity to produce the desired effect. The range gives physicians the choice of prescribing the herbs individually or in combinations to treat various ailments. The readily consumable form (capsules) ensures patient compliance.

Although primarily indicated for lifestyle disorders, Pure Herbs can be used for general maintenance of health and also in chronic disease management. In other words, it provides both preventive as well as curative benefits.

Salient Features of Pure Herbs

The Pure Herbs range is a unique range of potent herb extracts and is perhaps the biggest range of single herbs in the pharmaceutical market. More than half of the herbs in this range are for preventive use and can address problems of modern lifestyle such as stress, oxidative damage, and low immunity. These herbs are cost effective and can be safely consumed for longer durations. The herbs are packed in smart, user-friendly and portable containers. Each pack is contains 60 capsules and, keeping consumer economics and convenience in mind, is designed for one full month of supply.

The Pure Herbs Range

The Pure Herbs range includes amalaki as an anti-oxidant, arjuna for blood circulation, ashwagandha for anti-stress, bael for intestinal comfort, brahmi for alertness, bael for intestinal comfort, brahmi for alertness, gokshura for improving vitality, guduchi for immunomodulation, haridra for allergy care, kapikachhu for men's health, karela to regulate metabolism, lasuna for cholesterol protection, manjishtha for skin health, meshashringi for carbohydrate metabolism, neem for skincare, punarnava for urinary support, shallaki for joint pain, shatavari for women's health, shigru for joint care, shuddha guggulu for cholesterol regulation, sunthi for anti-nausea, tagara as relaxant, trikatu for gastric support, triphala as prokinetic cleanser, tulasi for cough and cold, vasaka for respiratory care, vrikshamla for weight control, and yasthimadhu for gastric care.
Salient features of Himalaya Pure Herbs

- Pure and concentrated herb in capsules with all attendant benefits
- Well-defined pharmacological activities
- Identification, determination, and validation of active compounds in Pure Herbs using HPTLC
- Identification of total marker profile in Pure Herbs with accuracy and specificity using LC-MS
- Scientifically tested to avoid batch-to-batch variation
- Guaranteed for the highest quality and potency

The Pure Herbs range

- Stimulate organic functions
- Possess therapeutic and nutritive values
- Improve and maintain healthy state of the body and mind
Cyperus rotundus, a pestiferous perennial weed with dark green glabrous culms, grows throughout India. *C. rotundus* has an elaborate underground system consisting of tubers, rhizomes, and roots. The tubers are white and succulent when young and hard and black when mature.

In traditional systems of medicine, tea made from the roots of *C. rotundus* has been used against jaundice. A study has documented that the extracts of *C. rotundus* showed significant virucidal activity against hepatitis B and cleared HBsAg, HBeAg, and HBV viral DNA copies, thus treating HBV infection. The extract was also found to improve appetite and renormalize liver enzymes, thus improving hepatic functions in patients with HBV infection.

Also, several other studies have shown that *C. rotundus* extract possesses wound-healing, stomachic, diuretic, demulcent, galactagogue, anthelmintic, antipyretic, analgesic, anti-inflammatory, antidiarrheal, anticariogenic, antiobesity, antihyperglycemic, neuroprotective, apoptotic, antibiotic, cytotoxic, antioxidant, and antiproliferative properties.

**References**


*C. rotundus* is used in Liv.52 HB

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Cyperus scariosus, a delicate and slender sedge, grows in the damp areas of Uttar Pradesh, Madhya Pradesh, and eastern and southern parts of India. The plant produces deep brown aromatic tubers.

Cyperine is the major active constituent of *C. scariosus*. The plant has been used in traditional systems of medicine for treating hepatobiliary disorders. A recent study showed that *C. scariosus* extract exhibited virucidal activity against hepatitis B virus (HBV). The extract of *C. scariosus* has also been found to renormalize liver functions in hepatitis B patients by optimizing alanine aminotransferase enzyme concentrations and offer hepatoprotective activity against the hepatotoxic dose of CCl4.

Also, other studies have shown that *C. scariosus* possesses antimicrobial, astringent, diaphoretic, diuretic, desiccant, cordial, stomachic, anti-inflammatory, antidiarrheal, antiviral, diuretic, spasmylic, hypotensive, bradycardiac, and tonic properties.

**References**


*Extract is used in Liv.52 HB
Withania somnifera

Withania somnifera is an evergreen, erect, branching shrub with fleshy and stout roots. The leaves are ovate with entire margin and arranged in an alternate fashion. Flowers are greenish in color, and fruits are small, round, and orange red when mature. W somnifera grows extensively in the subtropical regions of India, Nepal, Bangladesh, Pakistan, and Sri Lanka.

The major chemical constituents of W somnifera are steroidal lactones such as withanolides, withanine, and withaferin A; alkaloids like somniferine, somniferinine, somnine, tropine, cuscohygrine, pseudotropine, anaferine, isopelletierine, and anhydride; β-sitosterol, sitoindosides VII-X; and high amounts of iron.1

Root extracts of W somnifera have been widely used as an aphrodisiac and a geriatric tonic in traditional systems of medicine. A recent study reported that W somnifera possesses antioxidant property, which helps to reduce oxidative stress and improve semen quality.2

Another study showed that W somnifera brought significant relief from anxiety symptoms and improved mental health, fatigue, concentration, vitality, social functioning, and overall quality of life in patients with moderate-to-severe anxiety.3 W somnifera also possesses adaptogenic, anti-inflammatory, neuroprotective, neurodegenerative, immunostimulatory, cardioprotective, hypoglycemic, chemo- and radioprotective, and antiangiogenic properties.1

References

Asparagus racemosus

Asparagus racemosus, an under-shrub that grows up to 3 m in height is found throughout tropical Africa, Java, Australia, India, Sri Lanka, and southern parts of China. Stems of A racemosus are scandent, woody, and climbing; flowers are white with minute, purple anthers; and berries are globular or obscurely 3 lobed.

The principal constituents include saponins (Shatavarin I–IV), alkaloids, tannin, diosgenin, racemofuran, asparagamine A, racemosol,1 shatavaroside A, and shatavaroside B.2

In traditional systems of medicine, the fresh juice of root is given with honey as a demulcent in bilious dyspepsia or diarrhea. In Ayurveda, the root extract of A racemosus—a well-known tonic for feminine health—is prescribed to increase the milk secretion during lactation. Several studies showed that the administration of the extracts of A racemosus had galactagogue properties.3

Ethyl acetate and acetone extracts of roots of A racemosus inhibited spasmogen-induced contraction, while alcoholic extract specifically blocked the pitocin-induced contractions. The specific blocking of pitocin sensitive receptors, and not other uterine receptors, suggest that A racemosus could be used as uterine sedative.4

Several other studies have shown that A racemosus possesses antioxytocic5 and antiulcerogenic properties.6

References
What Do I Need to Know about Hepatitis B

What is hepatitis B?
Hepatitis B is a liver disease. The word “hepatitis” means “inflammation (irritation and swelling) of the liver.” Hepatitis B is a virus that causes inflammation of the liver. Inflammation can damage liver cells and cause the liver not to work properly.

What is the role of liver in human body?
Liver is one of the most important organs in the human body.

It does many important things to make sure everything runs smoothly:

- Stores nutrients and vitamins to help give your body energy
- Releases a substance called “bile” that helps in the digestion of fats
- Clears your blood of waste products, drugs, and poisonous substances
- Fights infections in the body.

How does hepatitis B virus damage the liver?
The hepatitis B virus (HBV) multiplies in liver cells. The presence of the virus triggers an immune response as the body tries to eliminate the virus and recover from the infection. This immune response causes inflammation and may seriously injure liver cells.

Hepatitis B can cause both acute and chronic disease. When a person first gets hepatitis B, he or she is said to have an “acute” infection. It occurs during the first 1 to 4 months after acquiring the virus. Some are not able to clear the virus and have “chronic” infection with hepatitis B, which is usually lifelong.

How do you get hepatitis B?
Hepatitis B is spread mainly by exposure to infected blood or body secretions.

You could get hepatitis B:
- By being born to a mother with hepatitis B
- By having sex with an infected person
- By using infected needles for injecting illicit drugs, tattooing, body piercing, or acupuncture
- By sharing toothbrushes and razors contaminated with infected fluids or blood
- Through blood transfusion.

You cannot get hepatitis B:
- Through food or water
- By casual contact: Shaking hands with, hugging, or sitting next to an infected person.

Hepatitis B cannot be spread through sneezing, coughing, or coming in contact with the feces of someone who is infected.

What are the symptoms of hepatitis B?
Hepatitis B usually has no typical symptoms or may cause flu-like symptoms. The symptoms can include:

- Yellowish eyes and skin, called jaundice
- Loss of appetite
- Nausea and vomiting
- Weakness and fatigue (feeling tired all the time)
- Abdominal pain, especially in the area around your liver
- Light-colored stools, dark yellow urine
- Diarrhea
- Joint pain
- Fever
- Easy bruising
- A longer than usual amount of time for bleeding to stop
What does it mean for my health?

Hepatitis B can cause:
- Chronic infection
- Cirrhosis (scarring) of the liver
- Liver cancer

What is chronic hepatitis B?

Hepatitis B is chronic (long-lasting) when the body cannot get rid of the hepatitis B virus. Children, especially infants, are more likely to get chronic hepatitis B, which usually has no symptoms until signs of liver damage appear. Without treatment, chronic hepatitis B can lead to scarring of the liver called cirrhosis, liver cancer, and liver failure.

How is hepatitis B treated?

Treatment for HBV depends on whether the infection is acute or chronic. Always consult your doctor for specific recommendations and treatment options.

Acute hepatitis B usually gets better after a few months.

Chronic hepatitis B is treated with drugs that slow or stop the virus from damaging the liver. The length of treatment varies.

How can I avoid getting hepatitis B?

- Vaccination
- Avoid sharing anything that can come in contact with blood or body fluids, such as razors, needles, and toothbrushes
- If you are getting a tattoo or body piercing, make sure the tools used are sterilized.
- Cover cuts, sores, and rashes with bandages.
- If you are sexually active, practice safe sex. Use a condom.
- Wear gloves if you have to touch another person’s blood or body fluids.
- Clear up blood or body fluids with warm water and detergent.

What can be done at home?

- Abstain from all alcohol intake if blood samples show that the disease is active.
- If you have chronic hepatitis B, you should be reviewed regularly in a specialist clinic because there are several treatment options.
- Eat a healthy, well-balanced diet.

Dear Doctor,

We hope you found this article useful for your patients. You can order for FREE reprints of this article by using the tear-out card enclosed in this issue, and use them as patient information leaflets in your clinic.

- Editor
Liv.52 Update

Role of Liv.52 in Viral Hepatitis

Gautam D.
Medical College and Hospital, Kolkata, India


Introduction
The term “viral hepatitis” refers to several forms of hepatitis caused by viruses. It is the most common type of hepatitis, a group of diseases that results in inflammation and damage of liver tissues. Viral hepatitis is often called infective hepatitis, as the causative viruses are contagious. The most common types of viral hepatitis include hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E. In India, viral hepatitis is an endemic disease assuming epidemic proportions occasionally. Although the majority of patients recover completely with no residual liver damage, a small number progresses to the chronic or fulminant form of the disease, resulting in death.

Modes of Transmission
Infection by hepatitis virus occurs after exposure to infected blood or other bodily fluids containing blood. This implies several possible modes of transmission, including parenteral, sexual, and vertical (from mother to child during pregnancy or birth). The most efficient mode of transmission is via blood transfusion.

Symptoms of viral hepatitis
- Jaundice
- Fatigue
- Abdominal pain
- Loss of appetite
- Nausea
- Diarrhea
- Fever
- Dark urine
- Relapse with cholestasis or serum sickness

Diagnosis of viral hepatitis
Diagnosis of acute viral hepatitis can be confirmed by the presence of IgM anti-hepatitis virus in serum. Baseline assessment should include hepatitis B serology (HBsAg/anti-HBs, HBeAg/anti-HBe), tests of disease activity (aspartate transaminase [AST] and alanine transaminase [ALT] levels), and disease severity (clinical evaluation; albumin, prothrombin, and bilirubin levels; and complete blood count). Viral replication (quantitative HBV-DNA measurement) should be measured in patients with evidence of active disease (elevated ALT) (A) (II). Liver histology, although not mandatory, is highly recommended in patients with active disease (A) (II). Patients with mild disease may not require treatment despite active viral replication. Molecular biology-based assays are invaluable tools in the management of chronic viral hepatitis. They can be used to diagnose active infection, establish the prognosis, guide treatment decisions, and assess the virological response to therapy. Serological investigations should be done only after appropriate pretest counseling and results should be given in conjunction with posttest discussion. Specific serological investigations are indicated in Tables 1 and 2.

Liv.52 tablet, a hepatospecific formulation from The Himalaya Drug Company, has a wide spectrum of therapeutic applications. It restores the metabolic efficiency of the liver in various etiological forms of hepatocellular jaundice, drug-induced hepatitis, and alcohol-induced hepatic damage. It also increases appetite and helps in the prevention and treatment of hepatitis and early cirrhotic conditions. It is a supportive treatment during hemodialysis and is a useful adjuvant with hepatotoxic drugs (eg, statins). Liv.52 is proven to be safe and effective by several clinical and nonclinical studies. Some of the various clinical trials conducted to evaluate the efficacy and safety of Liv.52 are discussed.
Table 1. Serodiagnosis of HAV and HCV

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Anti-HAV IgM</th>
<th>Anti-HAV total</th>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Anti-HBC</th>
<th>Anti-HBe</th>
<th>HBV-DNA</th>
<th>Anti-HCV</th>
<th>HCV-PCR</th>
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<td>Past hepatitis A</td>
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</table>

Table 2. Serological, Virological, and Biochemical Profiles of HBV

<table>
<thead>
<tr>
<th></th>
<th>HBsAg</th>
<th>Anti-HBs</th>
<th>Anti-HBe IgM</th>
<th>Anti-HBe total</th>
<th>HBV DNA (IU/mL)</th>
<th>ALT</th>
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<td>+</td>
<td>+</td>
<td>+/-</td>
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<td>Chronic HBeAg positive</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>High N</td>
</tr>
<tr>
<td>Immunotolerant phase</td>
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<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>High N</td>
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<tr>
<td>Immunoclearance phase</td>
<td>+</td>
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<td>+</td>
<td>-</td>
<td>+/-</td>
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<tr>
<td>Chronic HBeAg negative</td>
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<td>+/-</td>
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<td>+</td>
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<td>+/-</td>
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<tr>
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<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>N</td>
</tr>
</tbody>
</table>

+ = positive, - = negative, N = normal, ↑ = elevated

Clinical Trial 1

Efficacy of an Indigenous Compound, Liv.52, in Acute Viral Hepatitis—A Double-blind Study

Aim

Aim of the present trial was to evaluate the efficacy and safety of Liv.52 tablets in viral hepatitis.

Patients and Method

Inclusion criteria

Patients in the age group of 10 to 40 years who had jaundice for less than 10 days and serum bilirubin above 4.5 mg, and who were willing to give informed consent were included in the trial.

Exclusion criteria

Patients who had a history of ingesting hepatotoxic drugs prior to the onset of symptoms and who had HBAg in the serum were excluded from the trial.

Also, patients with rapid deterioration of liver functions, with signs of precoma and/or bleeding tendencies, and who were unwilling to give informed consent were excluded from the trial.

Study procedure

Patients with infective hepatitis were hospitalized during the acute phase of illness. Diagnosis was based on the clinical features of prodromata (anorexia, vomiting, malaise, and fever), highly colored urine and icterus, mild-to-moderate hepatomegaly, and elevated transaminases. Total 34 patients, who were randomized into two groups, received the treatment. Each patient received six tablets (two tablets TID) of the drug or placebo per day for 6 weeks according to the allocated group.

Results

A significantly shorter time for clinical recovery and for a 50% decrease in the levels of bilirubin was observed among patients in Liv.52-treated group. However, total recovery, evidenced by the normalization of biochemical parameters, took more or less the same time in both the groups. Although weight loss was recorded in 12 patients in Liv.52-treated group and in 10 patients in the placebo group, the degree of weight loss was significantly higher among patients in the placebo group.

Conclusion

A rapid amelioration of clinical signs and symptoms was observed among patients in Liv.52-treated group. Response to the drug was very much similar to that of steroids, but without side effects. Therefore, from the above findings, it can be concluded
that Liv.52 is an effective drug in the management of acute viral hepatitis, and more controlled trials should be conducted in patients with HBAg-positive hepatitis and progressive and chronic liver disease.

Clinical Trial 2
Liv.52 Therapy in Viral Hepatitis
Aim
Aim of the present trial was to evaluate the efficacy and safety of Liv.52 tablets in viral hepatitis.

Patients and Method
Inclusion criteria
Patients (of both the sexes) with viral hepatitis, and who were willing to give informed consent were included in the trial.

Exclusion criteria
Patients with carcinoma of the liver, and who were unwilling to give informed consent were excluded from the trial.

Study procedure
Fifty-two patients (including three patients with posttransfusion hepatitis and one with syringe hepatitis) were randomized into two groups, A and B. Patients in group A (25 patients) received antibiotics and steroids, and acted as controls, whereas patients in group B (27 patients) received only Liv.52 (2 tablets TID). Liver function tests, erythrocyte sedimentation rate, weight measurement, and urine examination were done for all the patients before and after the treatment.

Results
A significant improvement in the symptoms was observed among patients in group B (Liv.52) as compared to those in group A (control group). Improvement in appetite was observed within lesser number of days among patients in group B (average 5 days) as compared to patients in group A (average 9 days). In group B, reduction in body weight was observed in 16 patients, no change in body weight in two, and an average increase of 1.1 kg in 9 patients (33.3%). Relief from pain was observed after an average of 5 days in group A, as compared to 3 days in group B. In group A, constipation was reported in 10 out of 25 cases and needed mild laxatives or enemata, whereas in group B, constipation was reported in only 7 out of 27 cases and bowel movement returned to normal within 4 days of Liv.52 therapy, without any recourse to laxatives or enemata. No adverse effects were observed in any of the cases.

Conclusion
From the above findings, it can be concluded that Liv.52 can be effectively used in the treatment of viral hepatitis without any adverse effects.

Clinical Trial 3
Liv.52 in Infective Hepatitis
Aim
The aim of this trial was to evaluate the safety and efficacy of Liv.52 tablets in infective hepatitis.

Patients and Method
Inclusion criteria
Patients (aged between 15 and 50 years) with hepatitis, and who were willing to sign the informed consent were included in the trial.

Exclusion criteria
Patients with carcinoma of the liver, and who were unwilling to sign the informed consent were excluded from the trial.

Study procedure
Fifty patients were randomized into two groups, I (Liv.52) and II (control). Patients in group I (35 patients) were administered two tablets of Liv.52 thrice daily along with intravenous glucose, whereas patients in group II (15 patients) were administered 500 mg vitamin C twice daily along with intravenous glucose and corticosteroids. All patients were clinically investigated and liver function tests (serum bilirubin, alkaline phosphatase, and zinc sulfate turbidity) were done before treatment and after 7, 14, and 21 days of treatment.

Results
Relief from the symptoms of jaundice was observed in 23 patients (65.7%) in group I as compared to 7 patients (46.6%) in group II. Improvement in appetite was observed within 7 days in group I as compared to 9 days in group II. Abdominal pain was relieved within 2 days of Liv.52 treatment, while in group II it took 4 days or more. Nausea was relieved in 88% of patients in group I within 3 days of treatment, whereas it was present for more than a week in patients in group II. Fever subsided within 2 days and weakness and fatigue were ameliorated within a week of Liv.52 treatment. All patients treated with Liv.52 tablets reported a sense of well-being within a period of 3 days.

Conclusion
From the above findings, it can be concluded that Liv.52 improves liver function as well as the clinical, biochemical, and histopathological parameters. No side effect or toxicity was observed during the trial and none of the patients returned to hospital with relapse of jaundice.
Clinical Trial 4
Liv.52 in the Treatment of Infective Hepatitis, Chronic Active Hepatitis, and Cirrhosis of the Liver

Aim
Aim of the present study was to evaluate the safety and efficacy of Liv.52 tablets in infective hepatitis, chronic active hepatitis, and cirrhosis of the liver.

Patients and Method

Inclusion criteria
Patients with liver cirrhosis, infective hepatitis, or chronic active hepatitis had not received any treatment for these disorders were included in the trial.

Exclusion criteria
Patients with hepatic coma, aged below 10 years, and unwilling to give the informed consent were excluded from the trial.

Study procedure
One hundred and four patients were randomized into two groups, Liv.52 and control. Patients in the Liv.52 group (73) were administered four tablets thrice daily, whereas patients in the control group (31) were administered placebo drug. Hematological and biochemical investigations were done for all patients before treatment and at periodic intervals for 6 months.

Results
On analysis of the data obtained after the trial, the results were graded as “Good,” “Fair,” and “Poor.”

Category (1) Infective Hepatitis: Liv.52 was graded “Good” in 73.33%, “Fair” in 23.33%, and “Poor” in 3.33% of cases as against 26.66%, 66.66%, and 6.66%, respectively, in the placebo drug.

Category (2) Chronic Active Hepatitis: Liv.52 was graded “Good” in 37.50%, “Fair” in 50%, and “Poor” in 12.50% of cases as against 0%, 50%, and 50%, respectively, for the placebo drug.

Category (3) Cirrhosis of the Liver: Liv.52 was graded “Good” in 21.05%, “Fair” in 52.63%, and “Poor” in 26.32% of cases as against 0%, 37.50%, and 62.50%, respectively, in the placebo drug. No adverse effects were observed in any of the patients.

Conclusion
Treatment with Liv.52 has been found to be beneficial in patients with liver diseases. The drug may be considered a significant advance toward a successful treatment of chronic liver diseases.

Clinical Trial 5
Infectious Hepatitis—Study of 100 Cases

Aim
The aim of this trial was to evaluate the safety and efficacy of Liv.52 tablets and drops in viral hepatitis.

Patients and Method

Inclusion criteria
Children (of both sexes) aged between 2 and 12 years, with viral hepatitis, and willing to sign the informed consent were included in the trial.

Exclusion criteria
Patients with carcinoma of liver and unwilling to give the informed consent were excluded from the trial.

Study procedure
The present trial was conducted in 100 patients (all children) with viral hepatitis. Younger children were administered Liv.52 drops (20 drops thrice daily) and older children were administered Liv.52 tablets (two tablets thrice daily) for a period varying from 6 to 24 weeks.

Results
Results of the trial showed that addition of Liv.52 to the usual therapy resulted in faster relief from jaundice. Increase in appetite and a general feeling of well-being were observed in patients treated with Liv.52. There was a marked improvement in the symptoms of nausea, vomiting, anorexia, and abdominal pain. Pruritus was significantly relieved and the liver size and tenderness were decreased in patients treated with Liv.52. Biochemical parameters such as levels of serum bilirubin, serum alkaline phosphatase, AST, and ALT returned to normal. No adverse effects were observed in any of the cases.

Conclusion
Prolonged administration of Liv.52 in infective hepatitis would help restore the functions and metabolic processes of the liver.

Meta-analysis of 50 Phase III Clinical Trials in the Evaluation of Efficacy and Safety of Liv.52 in Infective Hepatitis

Meta-analysis conducted on Liv.52 included data from 50 clinical studies conducted over a period of 30 years in 4490 patients; this sample size was large enough for calculating the intervention (drug) effect. Of the total 50 studies, there were 3 double-blind placebo-controlled studies, 21 placebo-controlled studies, 22 noncomparative studies, and 4 case reports. The predefined primary end points were to determine level of statistical significance for the
following parameters: symptomatic improvement, renormalization of biochemical parameters, and total duration of clinical recovery. The predefined secondary end points were incidence of adverse events during the study period and compliance to the drug.

Of the 4490 patients in these 50 published studies, 3007 had received Liv.52 (Liv.52 group), 785 patients had received placebo, and the remaining 698 patients had received corticosteroids, multivitamins, or other treatments (patients receiving placebo or corticosteroids and other treatments comprised the control group). A total of 233 children (97 children below the age of 5 years, 117 children between 6 and 10 years, and 19 children between 11 and 15 years) were part of this meta-analysis.

Changes in the biochemical parameters (serum bilirubin [SB], serum glutamic oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], serum alkaline phosphatase [SAP], serum albumin [SA], serum globulin [SG], and prothrombin time [PT]) from baseline to the values at the end of the study, and total duration of clinical recovery were recorded. Incidence of adverse events during the study period and patient compliance to the drug treatment were noted.

The mean duration of these studies was 6.62 months and the total study duration was 331 months. A significant symptomatic control was observed in a week’s time among patients in the Liv.52 group. Cumulative analysis revealed a significant reduction in the mean levels of SB, SGOT, SGPT, and SAP and renormalization of protein levels and PT in the Liv.52 group. Also, there was a significant reduction in the mean period required for total recovery compared to the control group. No significant adverse events were reported or observed in these trials and the overall patient compliance to the treatment was excellent. Therefore, as per the predefined primary and secondary end points, Liv.52 is clinically, biochemically, and statistically proven to be effective and safe in patients with infective hepatitis. These significant effects might be due to the synergistic properties and actions of the ingredients of Liv.52.

Results of the above trials showed that Liv.52 is effective in the management of viral hepatitis. This effect may be due to the synergistic action of all the herbs used in the preparation. Liv.52 restores liver function, improves clinical, biochemical, and histopathological parameters, reduces ALT and AST levels, and thus effectively contributes to the role of a healthy liver in various important physiological body functions. It is safe for long-term use, has no contraindications and adverse effects. Thus, it can be concluded that Liv.52 is a safe, effective, practical, and affordable therapeutic modality in the treatment of viral hepatitis.

The Young Also Prone to Arthritis

It was supposed to be a condition affecting the elderly. Till a few years back, it was a common knowledge that joint problems spared the young but not anymore. According to latest research works, sedentary lifestyle and high prevalence of obesity have contributed to an increase in the number of patients suffering from osteoarthritis, a degenerative disease where cartilage of the joints wears out. People aged <35 years are being diagnosed with the disease, and many of them having to undergo joint replacement surgeries. There is a need for raising awareness about arthritis and maintaining a healthy lifestyle to keep the disease at bay.

Source: The Times of India. October 12, 2011
Online

Hepatitis B Foundation *Cause for a cure*
http://www.hepb.org/

The Hepatitis B Foundation is a nonprofit organization, solely dedicated to the global problem of hepatitis B. It is committed toward funding focused research, promoting disease awareness, supporting immunization and treatment initiatives, and serving as the primary source of information for patients and their families, the medical and scientific community, and the general public.

The Hepatitis B Foundation was established with personal support from Dr Baruch Blumberg, who won the Nobel Prize for his discovery of the hepatitis B virus. The Hepatitis B Foundation has grown into a professional organization with a global reach. Its goal is to improve the lives of those affected by hepatitis B through a comprehensive program of research, education, and patient advocacy.

Book

Hepatitis B: The Hunt for a Killer Virus
Blumberg BS

**Publisher:** Princeton University Press, 2003  
**ISBN-10:** 0691116237  
**Price:** US $25.95  
**Paperback:** 264 pages

With wit and insight, this scientific memoir and story of discovery describes how Baruch Blumberg and a team of researchers found a virus they were not looking for and created a vaccine for a disease they previously knew little about—work that took the author around the world and won him the Nobel Prize. Blumberg and his collaborators were investigating relationships between gene distribution and disease susceptibility, research that was yielding interesting data but no real breakthroughs. Through decades of hard work and investigative twists and turns, their pursuit led to the hepatitis B antigen, the elusive virus itself, and, ultimately, the vaccine. What Blumberg followed to the virus was a trail of remarkable “accidents” that happen when scientists seek answers to interesting questions. Those events, combined with the investigator’s determined persistence, resulted in studies that generated a pharmaceutical industry, have far-flung public-health applications, and saved millions of lives.
Crossword

Theme: Product names of The Himalaya Drug Company

Across
5. This drug is effective in the management of uterine disorders such as premenstrual syndrome, menstrual irregularities, and dysfunctional uterine bleeding. (7)
6. This product is a non-hormonal sexual stimulant for men. (6, 5)
8. A phytopharmaceutical formulation indicated for the treatment of senile and postmenopausal osteoporosis. (6)
9. A newly launched product that is recommended for the treatment of hepatitis B. (7)
10. It is effective in expelling kidney and ureteric stones and treating urinary tract infection. (7)

Down
1. It is helpful in the treatment of internal/external hemorrhoids, anal fissures, and varicose veins. (5)
2. A polyherbal formulation indicated for the management of diabetes and associated micro- and macrovascular complications. (8)
3. This phytopharmaceutical formulation is recommended for the management of common digestive disorders such as indigestion and gaseous distension. (5)
4. This drug is extremely useful in treating pollen allergy, allergic rhinitis, allergic bronchitis, and bronchial asthma. (6)
7. A product (available in 3 different forms—tablet, gel, and liniment) prescribed for the management of musculoskeletal disease conditions such as osteoarthritis, cervical and lumbar spondylosis, arthralgia, and gout. (8)
Shortly after the start of Mr Li’s first visit, my heart began to sink. He spoke Mandarin loquaciously, seemed fond of rambling stories, and complained of shortness of breath, dizziness, and headaches. Without the aid of an interpreter, I couldn’t understand his native language, which cascaded like an ever-flowing spring from his mouth, but I could see right away that he had a flair for the dramatic. His voice rose and fell like a hawk alternately soaring and diving through the mountain sky. His right hand waved expressively, making punctuation marks in the air. His hair, an unkempt pompadour with a mind of its own, danced and shook with each gesticulation. I made a mental goal of finishing the visit within 30 minutes.

Fifty-five minutes later, I stumbled out of the room, with a once-blank sheet of paper now completely filled with notes and lists of to-do’s for this gentleman. In my mind, I had him classified as a “challenging patient,” a challenge to my ability to manage the clock and stay on schedule, to my wish of obtaining clean and concise patient histories, to my goal of neatly packaging the problems of my patients. He had to return next week for follow-up, this visit with a double time slot.

He came back—3 months later. “I was out of town,” Mr Li told me. He did get some of the tests I’d ordered (the results were all basically normal), but he said that his previous symptoms were now gone. In fact, he had no complaints today. I couldn’t believe it. I felt like a college student just told that his organic chemistry final has been cancelled. As his friend, wearing an expensive-looking warm-up suit, looked on from the corner, I performed a focused examination. “Everything looks good,” I said. Just as I was about to shake the patient’s hand good-bye, his friend suddenly spoke up: “You know, he forgets a lot of things, like that last appointment. That’s what I’ve been really worried about. He used to be a heavy drinker, and now, he’s losing his memory.” Internally, I screamed like I was the subject of a painting by Edvard Munch. Externally, I tried to maintain my composure but couldn’t help but shake my head.

I slowly sat back down, wondering if my patient and his friend were conspiring to push me as far behind schedule as possible. His friend offered the additional history that Mr Li had few friends and rarely left his apartment. After gathering more details, I tested Mr Li’s short-term memory and found it to be quite poor. I ordered some tests and advised Mr Li to follow up with me in a week. After two visits, I basically had two mental snapshots of Mr Li, neither very flattering: the grandiloquent speaker with a propensity for making me tardy, and the former alcoholic who lived a solitary and memory-poor existence.

After several more visits, I finally felt like I had his medical issues—including his memory problems—reasonably addressed. Or did I? It had become very apparent to me just how poor his short-term memory could be. I began to worry about how he lived day-to-day at home, alone. Was he at safety risk? Could he take care of himself? Was he keeping his long list of medications straight? I tried to order a home-safety evaluation, but his insurance wouldn’t cover it. So I blocked out some time on my schedule to pay him a visit at home, the health care worker planning to assess the disaster scene.

Accompanied by an interpreter, I walked down the dimly lit hallway of his Chinatown apartment building. We arrived at his door, which was slightly ajar, and knocked. I expected to see a small, cramped apartment in disarray, with trash on the floors.
and medicine bottles everywhere. But when the door opened wide, I saw a clean, well-kept compact studio. Mr Li bowed as we entered after taking off our shoes at the door. “Ne hau?” I managed. “Thank you for allowing us to visit your home.” He smiled and said, “Not at all. Would you like some hot tea?”

After inviting us to sit, he turned down the volume on his television and sat down at the edge of his bed. With eyes sparkling and hands gesticulating, he talked about his addiction to television news, particularly coverage of Chinese politics. As I listened and sipped my tea, I was struck by how, in this setting, his inherent chattiness was rather charming. I also found myself comparing our dynamics here and in the clinic. Here, he was the host, at ease in his home, and he dictated the flow of conversation. At my office, I was the host, so to speak. But whether I was able to manage the flow of our visits was debatable, and this had been a source of frustration.

As we chatted, I glanced around. What caught my eyes was a series of dramatic black-and-white photographs along the walls, all of the same figure, captured in a variety of ornate Chinese costumes and equally ornate poses. The figure was of a young woman who obviously loved being in the camera’s eye. She looked hauntingly familiar. I had a vague recollection that, similar to Shakespearean plays in Elizabethan times, Chinese opera often used men in women’s roles. Could it be?

He was talking about how difficult it was to sleep in the heat of summer, without an air conditioner. When he finished, I commiserated with him, then said, “These are wonderful photographs. Who is that?”

“That was me,” he replied and cracked one of his infectious grins, the ones that made him look like a little boy up to his pockets in mischief. “That was when I was very young. I sang in the Chinese opera.”

As we talked further, I learned that he had been quite a famous opera star in his 20s to 40s, even nationally renowned in China. Despite his humble apartment and his rambling histories in the office, I was somehow not surprised. In fact, it all seemed to make sense now. His dramatic stories and gestures, the musicality of his speaking voice, his larger-than-life facial expressions… one could describe them all as “operatic.”

By the end of the home visit, about 30 minutes later, I had accomplished my goal of assessing his living situation. I’d found that safety bars were already installed in the bathroom, that his medicine bottles included two different PPI’s, and that he liked to keep his stove on all day to keep water warm for his tea (which had led to a couple of stove fires). Subsequently, I was able to help arrange for a caregiver to assist with shopping and meals, and provide a new electric hot water heater. It is easy to see how these interventions have an equal, if not greater, impact on his health and well-being than, say, getting him to his target cholesterol level.

Somewhat unexpectedly—because I hadn’t given it much thought beforehand—I also gained a glimpse of his life away from the stage, that is, the physician’s office. What a privilege to be allowed into his home, to be given a brief view of his personal history. I have come away with a new appreciation and respect for his colorful ways. What once made me feel impatient now strikes me as endearing. Our subsequent clinic visits, at least from my perspective, have been quite enjoyable. We have developed a strong rapport on mutual respect and shared sense of humor. And with better rapport, came deeper understanding, heightened empathy, and an improved ability to manage our visits. When he comes into the office with a list of four health complaints but still has that grin, I know that I probably don’t need to hit the panic button and order a bunch of tests. I know that if there’s an important medical appointment or test he needs to have, we should call him the day before to remind him. I know that when he says that everything is “Bu cuo,” or not bad, that means he’s doing really well.

I’ve learned that spending time with him, in this relationship of trust, is an honor—even if our visits still run overtime.

With the time pressures of today’s health care scene, it is easy for me to focus only on the here and now in the 10 or 15 minutes allotted to see each patient. Viewed in the present tense only, a patient like Mr Li can appear a time management challenge, even a nuisance. Once I learned more about his life “backstage,” I was able to replace my cartoonish mental impressions with a picture of more substance and an understanding of more depth.

There are patients with whom I feel an instant connection, and those who present more of a challenge in terms of the patient–physician relationship. It seems to me that I tend to ask the former more about their lives outside the office. But shouldn’t it be the other way? My experience with Mr Li showed me that learning about the personal history of a “difficult” patient can transform the relationship. Contrary to my natural instinct, it is especially with the problematic patient that I should actively seek out this information. With Mr Li, it was worth the extra effort—and the extra time.
Judd was 10 years old when his mother died. After she died, his father brought Judd and his two older brothers back to the hospital to be with their mother one last time and to recite the 23rd Psalm. After the Psalm had been read, the family left the hospital room. Judd hadn’t gotten too far down the hallway before he suddenly returned to her room. Holding onto the doorway with his small hands, he leaned into the room and said strongly, “Bye, Mom.” It was not a final good-bye. It was a good-bye saying, “I’ll see you again real soon, like tomorrow.”

Judd’s mother was not a patient of mine, but I knew a little bit about her medical history. Judi was as healthy as the proverbial horse until, for no obvious reason, she developed vaginal bleeding that exceeded her normal menstrual flow. She first became alarmed when, one day, the blood soaked through her dress.

Her gynecologist ordered some blood tests. After obtaining the results, Judi’s mother exclaimed amusingly, “My platelets are low. I need platelets, little plates that will complete my 12-plate china setting!” At home, her school degrees were proudly displayed in the laundry room, where, she figured, she spent most of her time anyway. Her humor was everywhere, really. The psychologist in her could not resist needle pointing the following, which she kept in the kitchen, “before I had children, I had three theories about bringing up children. Now I have three children and no theories.” On the wall right above this was a plaque with another message, “I hope my children look back on today and see a mother who had time to play. There will be years for cleaning and cooking for children grow up—when we are not looking!”

You know, she took that to heart. You could feel it in the journals she wrote to each of her three children during the last week of her life. To Judd she wrote, “Judd, my precious baby, always smiling, always happy. That I was able to name you Daniel (as your first name) after your grandfather, great uncle, and great-grandfather was a treat. Then to have you named Judi for me was nice too. You, my Judd, were beautiful, and you were my last baby, so I wanted to savor your specialness.”

On Judi’s first hospital day, a bone marrow biopsy revealed acute myelogenous leukemia. Despite this life-threatening diagnosis, her mood was upbeat. Friends visited. Her room could not accommodate all of the flowers that were being sent, and they started to line the countertops of the nurses’ station. Get-well cards were delivered during the day. While Judi slept, visitors’ books were signed by family members, students (after all, she had been running a support group at one of the local high schools for students who had lost a family member), and acquaintances. Fortunately, multiple transfusions stopped the bleeding. Unfortunately, intravenous chemotherapy (ordered to eradicate her cancerous stem/blast cells) proved to be too destructive. Her resistance disappeared, leaving her vulnerable. Though her defenses were down, she struggled on. About 10 days after being hospitalized, she shocked her husband by bringing up the prospect that she might die. In his presence, she wondered aloud how he and “the boys” would get on. Too stunned to say much, he offered very few answers to her questions and concerns.

A few days later, her husband brought to his wife’s hospital room a meal consisting of Thanksgiving Day turkey with all the trimmings, served on their best china, including a small butter plate—a “platelet.” Although excited for the moment, Judi was weak, but not too weak to return her husband’s kiss, their cheeks touching ever so softly. Two days later, instead of going into remission following her 2-week course of chemotherapy, her condition worsened. A heart rate of 200. It couldn’t be. Sepsis? Being intubated, Judi couldn’t speak. Perhaps realizing that the speed of her heartbeats was reflecting her dire condition, she wanted to calm her anxiety, reduce her rapid heartbeat—anything to slow down the runaway train. Deliberately and legibly, she wrote “Valium” on her stencil board. It didn’t help. Soon afterward, her heart stopped beating.

After leaving the hospital that day, Judd, my youngest son, never saw his mother alive again. That’s something for the future. After all, he was just saying “Bye, Mom” for now—not forever.
Mr M. Manal forms The Himalaya Drug Company. His vision: put Ayurveda on par with modern medicine.

1930

Launch of Serpina®, the world’s first natural antihypertensive drug, derived from Rauwolfia serpentina.

1934

Dr Roshan M. Captain Ph.D., joins the company and spearheads research and development.

1950

Liv.52®, a hepatoprotective, is launched and goes on to become one of the world's top-selling herbal drugs.

1955

Located in Bangalore, India, Himalaya’s 70,000 sq.ft Research & Development Center is a world-class facility engaged in advanced research in herbal medicine and specialized herbal cosmeceuticals. With a team of over 130 multidisciplinary scientists, the R&D team carries out pioneering research aimed at developing safer and effective medicines that improve the quality of life.

What does the R&D team do?
The R&D team conducts studies on natural products to determine efficacy of herbs, authentication, standardization, isolation of new molecules, structure elucidation and stability studies, and safety and efficacy in preclinical and clinical situations.

How is a product developed?
Each Himalaya product goes through more than 6 to 8 years of research before being launched. Therapeutic products are subjected to the same rigorous standards of testing as any allopathic drug including toxicity studies, Phase I to Phase IV clinical trials, and stability studies. The clinical trials are based on Helsinki Declaration and protocols adhere to WHO and Good Clinical Practices (GCP) standards.

Clinical trials
The Himalaya Drug Company has conducted clinical trials at leading hospitals in India and overseas, including All India Institute of Medical Sciences, Delhi; Apollo Hospitals, Chennai; St. John’s Hospital, Bangalore; IMS BHU, Varanasi; Mayo Clinic, Rochester, United States; Central Institute of Tuberculosis of Medical Academy of R.F., Moscow, Russia; Novosibirsk Research TB Institute, Russia; and Charles University, Prague, Czech Republic. Himalaya has more than 1000 research papers published in leading international journals such as Journal of the American Medical Association (JAMA), Alternative Medicine, Indian Journal of Medical Research, The British Journal of Radiology, Australian Journal of Herbal Medicine, and Journal of Ethnopharmacology.

Research and Development and patents
In less than 10 years, the R&D team has filed 85 international (global) patent applications and has gained 7 patents, making the company one of the leading herbal medicine researchers in India. Currently, research work at Himalaya includes the discovery and development of potential drugs for obesity, diabetes, cancer, women’s health disorders, AIDS, and other infectious and viral diseases.
Corporate Social Responsibility

Corporate social responsibility forms an integral part of The Himalaya Drug Company, which believes in caring for the planet and people.

At Himalaya, herbs are grown organically—without using chemical fertilizers or pesticides in farming. Herbs are grown eco-sensitively (protecting the earth) so that they can be harvested with all their natural goodness.

The Himalaya Drug Company has also received the ISO-14001:2004 certification—the most recognized standard, globally, for environment management. A rainwater harvesting project has been set up in the company for making efficient use of rainwater. By channelizing the flow of rainwater through percolation trenches into an open abandoned well, daily requirement of water are met through this system.

A network of over 3,000 farmers across India is working for The Himalaya Drug Company to cultivate herbs using good agricultural practices. Apart from this, it has engaged the Soliga tribe of South India to collect certified organic forest honey. The company supports more than 1,000 families of registered traditional honey collectors through the honey collection project.

Recently, the company has tied up with a prison rehabilitation center in Bangalore to engage inmates for a farming project, in which they will grow medicinal herbs for various needs of the company. The company will train the inmates on farming methods and practices, which will enhance their chances of employment even after serving their jail term.

The company believes in reducing carbon footprint as much as possible. Its green packaging policy focuses on two main areas—minimizing the use of packaging materials and replacing existing packaging material with eco-friendly packaging. It has partnered with the US-based international tree-planting organization, Trees for the Future, to plant trees across India. The company has planted over 150,000 in 3 years. Each tree on an average offsets 50 lbs of CO₂ (carbon dioxide) per year.

Himalaya receives Good Laboratory Practice (GLP) certification for adhering to toxicity guidelines in nonclinical safety studies.

Mr Meraj Manal, the founder’s son, joins the company.

Mr Karstein, a German pharmaceutical consultant, directs the company’s focus towards conventional medical practitioners.

An advanced manufacturing facility is set up in Bangalore. This facility later expands to become the corporate headquarters.

Himalaya’s Research & Development center moves to Bangalore.

The company opens its US office in Houston, Texas.

World Health Organization (WHO)-Good Manufacturing Practice (GMP) certificate given to Himalaya for its manufacturing facility in Bangalore.

2009

2010

1964

1965

1975

1991

1996
While making rounds, a doctor points out an x-ray to a group of medical students. “As you can see,” she says, “the patient limps because his left fibula and tibia are radically arched. Michael, what would you do in a case like this?” “Well,” ponders the student, “I suppose I’d limp too.”

“I finally quit smoking by using the patch. I put six of them over my mouth.”

Patient: Doctor, what does the x-ray of my head show? Doctor: Absolutely nothing!

Overheard in a busy clinic as a receptionist spoke to an obviously hard-of-hearing client: “No Mrs Smith, not the HEARSE, I’m sending the NURSE!”

Patient: These tablets have a very funny effect on my bowels. Surgeon: What are they? Patient: Ferocious sulfate.

Patient: How much to have this tooth pulled? Dentist: ₹30,000.

Patient: ₹30,000 for just a few minutes work? Dentist: Well, I can extract it very slowly if you like.

The young man was quite adamant. He insisted to the surgeon that he wanted to be castrated. The surgeon pointed out that this was a drastic step for a young man to take and strongly urged him to reconsider his request. “No,” said the young man, “I have thought long and hard about it, I have read all there is about it and have made up my mind. I must have the operation.”

The operation was duly carried out and when he had recovered from the anesthetic and was back in the ward he got to talk to the other patients. “And what are you in here for?” he asked the fellow in the next bed. “To be circumcised.” “Damn, that was the word I meant!”

Patient: “I can’t decide whether to slash my wrists, or blow my brains out.” Psychiatrist: “You have difficulty making decisions.”

Think Wise
He who controls others may be powerful, but he who has mastered himself is mightier still.
– Lao-Tzu

Your Feedback Matters to Us!
We would like to hear from you on this special issue of Probe. Please write to us with your views at publications@himalayahealthcare.com
Scientific Publications from The Himalaya Drug Company
Celebrating 50 years of
Liv.52
Septilin
Speman
Cystone
Gasex
Lukol
Rumalaya
Herbolax
Tentex forte
Styplon
Pilex