CHIEF EDITOR DR. SYED MUBIN AKHTAR

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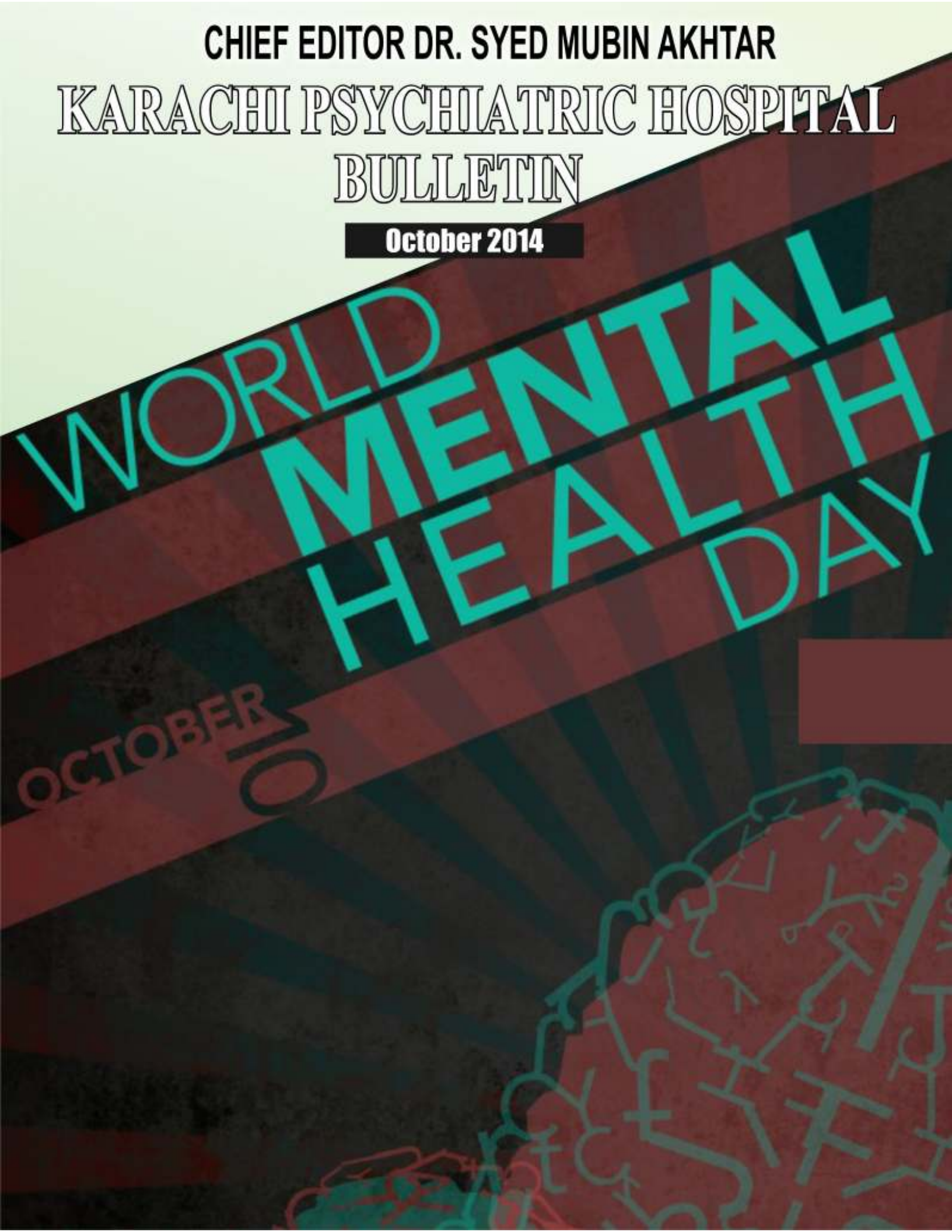
WORLD MENTAL HEALTH DAY

OCTOBER 10



Eid Millan at Karachi Psychiatric Hospital

On the occasion of world suicide day Managing Director Dr. Syed Mubin Akhtar ,
Prof. Iqbal Afridi, Directors of kph Kausar Mubin, Syed Salahuddin, Mehjabeen Akhtar, Mahrukh Akhtar, Abdur rehman, Haider Ali, Dr. Akhtar Fareed Siddiqui and CEO Rashid Hasan adressing the audience at Karachi Psychiatric Hospital.

Employees of K.P.H. are attending the Eid Milan party.

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Stories on Sita White, narcotics use,alleged affair with 21-year-old, other comments and programmes caused Imran's annoyance: Jang, Geo Group

Spokesperson says when a reporter asked Imran to provide a sample of his blood test to reject the charge of taking drugs, the PTI chairman got infuriated; he begins speeches with recitation from Holy Quran but degenerates into foul language; when logic fails, it is easy to brand people as traitors and agents of Jews, Americans and Indians; Imran assigned target of defaming Jang Group; in his speeches and interviews, he repeatedly and purposely accuses Jang Group of being anti-army whereas the fact is that Jang Group loves the army; PTI chief got offended when he was issued the first notice on his baseless cricket rights allegation; Jang Group has moved courts on all allegations levelled by Imran; spokesperson challenges Imran that as he does not trust Pak courts, he should repeat all allegations in UK where courts will decide quickly on who is right; his KPK govt has banned Jang, Geo Group ads since April; is this his vision of a new Pakistan?

The spokes person of the Jang/Geo Group has rejected the allegations levelled by Mr. Imran Khan against the Group and has stated that these unfounded and baseless allegations have been repeated many times and the answers to his mindless tirades are available on the Group's website.

Mr. Imran Khan seems to have taken a leaf out of the fascist propagandist, Goebbels, who served as Hitler's information minister. Goebbels infamously believed that if a lie is told persistently and repeatedly it is soon perceived as the truth. Mr. Khan has been audacious in his attacks which reveal an arrogant and stubborn mindset created by misplaced narcissism. This is unfortunate. Pride often goes before the fall, the spokesperson said.

The language Mr. Khan has employed has descended to the gutter level. His speeches are full of expressions that are normally associated with the bazaar. Note some of them: I will hang them upside down. I will drag them out of their homes by force. I will hang them with my own hands. I will throttle them with my bare hands. They are trembling with fear and have wet their pants. Shame on you! This is hardly the language expected of a leader. The tone and tenor is threatening and full of incitement to violence and mutiny. The irony is that he begins his speeches by reciting the verses from The Holy Quran and then stoops to the level of the gutter.

The Quran says that one of the primary qualities of a leader is his soft tone and manner. Perhaps Mr. Khan has been affected by his domestic crisis and political failure. There can be no other explanation for his irrational behavior, the spokesman added. Thosewho are claiming to be the architects of a New Pakistan have not only targeted the Jang- Geo Group, their venomhas also been directed at honorable parliamentarians, judges, bureaucrats, police officials and people with impeccable reputations.

The people of Pakistan are bewildered by this bizarre behaviour. How can people who are constantly sermonising and lecturing the masses about values and culture stoop to such a level, the spokesperson asked. Mr. Imran Khan is neither a partner nor shareholder in our Group, nor does he have a dispute with us in this regard. He seems to have developed the same complaints and grudges against us that all previous governments and powerful groups have harboured against the Group. "These complaints are not about disputes over money or claims on property. Their anger has always been directed against our independent policies and journalistic ethics.

"Their wrath is against our pursuit of the truth and our speaking truth to power. Despite their opposition we have always tried to give all parties a chance to defend their position and have incorporated their version in our stories." Mr. Imran Khan does not want to face independent journalists. He has been told that he should avoid attacking the journalist fraternity as it could backfire. He has therefore, decided, as a strategy, to attack our brand and our senior management because he believes they are easy targets and may not retaliate. Surely, he is aware that every line published in our newspapers and every story broadcast on our TV screens is the result of the hard work and dedication of our journalists.

The independence of our journalists is recognised and is often quoted as an example of genuine freedom of expression. We are proud of this legacy, the spokesperson said. When Mr. Imran Khan says that he has no complaints against journalists, he is not telling the truth. His real grudge is against journalists and their probing questions that dent his carefully built facade. Mr. Khan has complaints against four of our journalistswhowork for our newspapers and channels. He has openly asked us to rein in these journalists. He then categorically demanded that these journalists should apologise to him.When these demands were not met in the interest of free speech, he insisted that we sack these journalists.

This is the true story of his much trumpeted great love for journalists, the spokesman commented. The spokesman said that Mr. Khan has had grievances against the Group in the past but these were resolved after discussion and debates in a civilised manner. However, in recent times his attacks have become more vicious and unreasonable. There is a reason for this and perhaps it is time to remove the veil and look at the real motives behind his tirades. After certain incidents in the recent past, a campaign to destroy the Jang-Geo Group was initiated.

The strategy was to avoid any direct attack on journalists and to concentrate all attacks on the management and other responsible personnel of the Group. The plan was to defame, discredit and destroy the reputation of these individuals. They wanted to lower us in the eyes of the general public and taint us. Mr. Khan was told to join this ongoing campaign of vilification and add his voice to the hate speech emanating from certain quarters.

Once he joined this coterie of powerful people, Mr. Khan's tone and demeanor changed. His language became a reflection of his handlers as he began to level the same allegations and peddle the same unfounded accusations with great zeal. He parroted the voice of his partners in crime to the point of caricature. He became an echo. He also called us traitors. He did not realise that we had served a legal notice on those forces that had accused us of treason.We have waited for four months and not a shred of evidence has been provided to us.

It was not an easy decision to serve a legal notice to such a powerful organisation. Only a group that is confident that it has nothing to hide would take such a step, the spokesman said. "We have no other choice but to also take Mr. Khan to court." Mr. Khan has alleged that we receive funds from abroad to pursue a foreign agenda. One of the allegations is that we are receiving funds fromabroad, especiallywith regard to our Aman ki Asha campaign.

The fact is that this allegation of the receipt of foreign funds was proven wrong in the Supreme Court of Pakistan. The whole world knows that Mr. Khan has close relationships with foreign countries and foreigners and receives funds from them for his activities. Those funding him remain anonymous.

He has received billions of dollars from institutions and individuals in the US and UK and has never disclosed the source of his funds. We are the only media group in Pakistan that Washington has complaints against.Mr. Khan can find evidence of this in the documents exposed byWikiLeaks. He should be aware that our policies are never based on ad-hocismor opportunism. We pursue

longterm goals which are coherent and consistent. We have no hidden agenda. Our only agenda is Pakistan - a better, prosperous and stable Pakistan. This is why we have credibility and the people have unshakable trust in our brand. The spokesperson strongly rejected the allegations levelled byMr. Khan that the Group ran a campaign against the armed forces of Pakistan.

If Mr. Khan had made the effort he would have realised that our group has done countless programmes extolling the heroism and bravery of our armed forces and has always stood by them in every hour of trial, the spokesperson said. He would then have understood how deep our love and respect for the armed forces is and has always been. Mr. Khan and his cohorts have been given the target to create disharmony between our Group and the armed forces and to create confusion among our viewers and readers. His attempt to make us controversial will not succeed, the spokesperson added. The internationally renowned institution, Fair and Free Election Network (Fafen) has rejectedMr. Khan's allegations that Geo was involved in election rigging, yet Mr. Khan continues to repeat this allegation like a broken record. "His ludicrous allegations that we were in league with Mr. Nawaz Sharif in rigging the election is a blatant lie.

If Mr. Khan had bothered to look at the Fafen report, available on our website , he would realise how absurd his allegations were," the spokesperson added. The spokesperson said that Mr. Khan was being misled by certain forces. His allegations that the Group has had got any taxes exempted by the Nawaz Sharif government is totally baseless. He has threatened to take back every penny from our so calledwindfall and vowed to shut us down if he comes to power. This 'friend' of journalists should think twice before threatening the livelihood of thousands of journalists in our Group. Instead of exposing thosewho have tried to shut us down and brought us to the brink of financial ruin, Mr. Khan has chosen to stand with those very forces.He shares their aim to destroy our Group.

This is the same Group which was showered with praises by Mr. Khan in the not too distant past. He often said that he was a fan of our Group. "With a friend like this who needs enemies," the spokesperson wondered. Mr. Khan avoids attacking journalists but has attacked the edifice that sustains their livelihood. This is all part of a nefarious design and Mr. Khan has chosen to implement it. He is cutting the very tree under whose spreading branches so many from the journalist fraternity have found shade and solace and shelter His allegations that the Group has evaded taxes are laughable and shoddy. The tax authorities know how much tax we pay.

They know how to extract taxes from any tax thieves. It is one of our cardinal principles that we cannot remain independent if our financial matters are not in order. Our relationships with governments have always been turbulent because of our independent reporting. If we were tax evaders, governments would be able to squeeze us and dent our independence and credibility. Mr. Khan does not know his history. If he did hewould not make such spurious allegations. Mr. Khan has alleged that when, in his previous tenure as PM, Mr. Nawaz Sharif served us with tax notices, we made it an issue of freedom of expression to extricate ourselves from alleged financial wrong doing.

Once again,Mr. Khan is ignorant of history. He should have asked the witnesses of this episode about the facts. He would then understand the truth. For this he does not have to go very far. He needs to just ask Shaikh Rasheed and Mushahid Hussain, who have intimate knowledge of the entirematter. Theywere eyewitnesses to the whole affair. The Jang Group took the matter to the Supreme Court. All journalists' bodies, political and social activists, lawyers and especially the people stood by us against this assault on free expression. It was through their support and pressure that the matter was resolved. This is all part of the historical record. For the information ofMr. Khan, certain senior members of Mr. Sharif's cabinet tried their best to incriminate us.

This was acknowledged by Mr. Sharif who apologised for it. In the recent past, Mr. Zardari and his predecessor General Musharraf both tried to punish us for our independent reporting. Virtually, 99 percent of our advertisements were blocked. They put hurdles in our path fromtime to time andMusharraf shut down the Geo TV Network for threemonths. They disrupted cable transmissions on numerous occasions and caused us losses of billions of rupees.

We have gone to the courts for relief. During Mr. Zardari's tenure, we were accused of asking for Rs4 billion from his government. Mr. Khan acknowledged this in his many statements and praised our Group for not bowing to pressure.We have shown clips of his views on this subject on Geo. Mr. Khan has threatened that once he comes to power, he will sort us out. We say this with all humility that he can try. We are prepared because we have no skeletons in our cupboards. We have weathered many a storm. Field Marshal Ayub Khan, General Zia ul Haq, Nawaz Sharif, General Musharraf and Asif Zardari have all tried and failed to make us cower in fear and compromise. History tells us that our Group stood and fought for the principles enunciated in the constitution.

We have always kept the interest of the public supreme and have suffered financial losses as a consequence. In every era there have been some who have been happy with us and some who have been upset and angry with us. The spokesperson said that Mr. Khan had grievanceswith the Group in the past but his new found annoyance stems from some recent events. One of them relates to the coverage given to Arsalan Iftikhar who made new revelations about Mr. Khan's alleged love child in various forums. These allegations were printed in all newspapers and broadcast on all TV channels.

Our journalists also investigated this matter and pointed out that this was an old case in which an American court had given its ruling on a complaint lodged by Mr. Khan's alleged girlfriend, Sita White. The story with the background, new revelations and Mr. Khan's and his party's version was printed and broadcast. However, Mr. Khan's anger at this story shows of no sign of abating. He was also upset about factual investigative reports about his government's performance in KP. Instead of defending his position with logic, reason and facts, as he does with the foreign media, Mr. Khan reacted by bestowing on us the epithets of Pharoah and blackmailer.

In doing so he set aside verses of The Quran, Islamic injunctions and legal norms thereby reducing his stature as a leader, the spokesperson said. Unfortunately, this is a common trait in our society. When losing an argument it is easy to launch into abuse and invective. Once we have no evidence or when logic and reason fail us we try to intimidate our opponent by using foul language. We hurl all sorts of allegations at the other party. It is also common to call an opponent an agent of America, the CIA, Raw, the Jews and tax thieves. When President Nixonwas exposed by theWashington Post in the Watergate scandal, he did not resort to abuse, he used other means to try and stop their coverage.

Another incident that irked Mr. Khan was a re-tweet by one of our journalists about an alleged affair between a 21-yearold girl and a politician. No names were mentioned. Mr. Khan spoke of this re-tweet in one of his rallies. His intention was to rally his supporters against our Group but his words spread like wild fire. What was once drawing room gossip was now being discussed on the street. Mr. Khan's supporters complained to us and protested. We explained that we were not involved and the re-tweet was the journalist's own doing in his personal capacity. We also told them that a similar story was filed by one of our reporters but we did not print it because he did not have any substantive proof and Mr. Khan's version was not included in his report.

They insisted that we take action against our journalists. We told them, in all sincerity, to pursue the matter in court. They did not do so. Instead they trained their guns against our Group. Another reporter was working on a story about rumours of Mr. Khan's use of narcotics.He asked Mr. Khan whether he took any narcotics and if he was prepared to take a blood test to lay rumours about his addiction to rest. Mr. Khan called our senior editor and angrily protested against this intrusion in his private affairs. The senior editor asked him to control his temper and be more tolerant. He reminded Mr. Khan that being a public figure he should accept being under scrutiny. He was told that people were interested in his private life and have a right to know about their leaders. Mr. Khan remained adamant and angry.

The story was not published. The spokesperson said that Mr. Khan is also upset with the Group because it had exposed his boast of bringing 10 lakh people to the Dharna. Hewas unable to bring in the promised numbers and his sit-in has a fewthousand participants. For our assessments we relied on the number count given out by the government, ministry of interior and the police. However, in the interest of balance we also broadcast and printedMr. Khan's inflated claims. This balanced and fair reporting was obviously not to Mr. Khans liking, the spokesperson added. Mr. Khan has boycotted our Group. Despite this we have not refrained from giving his activities space and time.

His supporters have not told him that this ploy of boycotting our Group is not new and has been used several times in the past by powerful sections of the power elite. They should have known that this achieves nothing. We have emerged from such boycotts stronger and more determined, by the Grace of Allah, the spokesperson said. If Mr. Khan and his party refuse to give us their version and walk away in a huff we can only pray for them and hope they see the light. If he continues to boycott and also complain about one sided reporting, he has only himself to blame. We have not censored anything he has said, no matter how hurtful and libelous.

The spokesperson wondered whether Mr. Khan had lost all sense of balance. He seems to vacillate between the extremes of love and hate. He sings the praises of a person when it suits him and then curses the same personwhen things do not go his way. He was once close to General Musharraf and even accepted dogs from him as a present. But when he was not made prime minister he became the sworn enemy of the general. His hatred for Altaf Hussain crossed all boundaries at one time and then suddenly all the animosity evaporated. When he attacked Mr. Zardari, he was vicious and relentless but as soon as he took on Mr. Nawaz Sharif, he said Mr. Zardari was a thousand times better than Mr. Sharif. When he was enamored of Mr. Sharif, he happily asked and accepted a plot

from him but when his amour faded he wanted nothing less than his head. When he praised former CJ Iftikhar Choudhry, he never ran out of positive adjectives. When he fell out of love with the former CJ, he hurled the choicest abuses at him. Recently, in his reply to a legal notice served on himby the former CJ,Mr. Khan praised him to the skies and then in yet anothermanifestation of his erratic behaviour he withdrew his words and attacked him. Nobody knows when he will turn. His u-turns and about turns are now perfect material for parody, the spokesperson commented.

The spokesperson asked the people to be the judge. Our Group has a policy to keep the public abreast of all events and to provide them with all shades of opinion. This is the best way to serve an inclusive Pakistan. Unlike Mr. Khan we do not twist and turn in the wind and change to suit the occasion. We are not opportunists. He has asked the people to stop watching Geo, boycott our publications and has gone to the extent of asking our staff to abandon the Group. He has urged advertisers to stop giving us business. These are old tactics. We have been subjected to these ploys before.

Our consumers will determine what is good for them. Not Mr. Khan, said the spokesperson. We have toldMr. Khan on numerous occasions to take his complaints to the Press Council, Pemra or the courts. It is strange that he avoids us in court and has resorted to delaying tactics in cases we have filed against him. He continues to rave and rant in rallies and interviews against our Group without evidence or proof. We are printing our legal notice and his reply so that our readers can draw their own conclusions about what is right and who is wrong. They will understand that the person who grows hoarse calling for justice and insaaf wants a selective form of insaaf for himself.

The scales of justice in his hands are deliberately kept imbalanced, the spokesperson said. We have only one request, said the spokesperson. Let us pursue the matter in the courts. Mr. Khan, kindly, instruct your lawyers not to obstruct the flow of justice. Let the truth come out in the open. Mr. Khan seems to have lost confidence in the courts of Pakistan. We suggest that on his frequent trips to London, Mr. Khan should repeat his allegations, word by word, and have them printed in a UK newspaper or broadcast on a UK channel. He has always praised the systemof justice prevailing in England and knows that the courts there do not delay their judgments, especially in defamation cases. We will then take himto court in the UK and justice will be served expeditiously. Allah grants respect to whomsoever He pleases and disgraces whomsoever He pleases.

The spokes person said that Mr. Imran Khan accuses us of launching a campaign against the former additional secretary of the ElectionCommission of Pakistan. The spokesperson said that we only presented the facts including the photograph which shows Mr. Afzal Khan carrying a PTI flag in the recent dharna. There are more photographs available with us, proving his affiliation and partisanship with the PTI. Mr. Afzal Khan has admitted in his infamous interview that he had no proof at all to substantiate his sensational allegations. Besides, Mr. Afzal Khan in many interviews available with us has praised the entire election process both before and after the elections.

We merely showed clips of these claims of election transparency to show his hypocrisy. Inmore than one interviews, he claimed that the elections were the fairest ever. He also showered praises on former chief justice Iftikhar Chaudhry. Jang and Geo merely exposed Afzal Khan and his blatant lies. The spokesperson further stated that Mr. Khan's cronies continue to carry out vicious propaganda against the group on social media using different names and hiding behind anonymity. The spokesperson appealed to the people of Pakistan to beware of these tactics. Mr. Khan calls the management of the Group a people without conscience.

If bringing forth unpalatable truths is evidence of our being conscienceless,we happily accept this title.Wewill continue to pursue the truth in the interest of Pakistan. Please keep in mind, the spokesman said, that GEO has been virtually shut down for almost four months. This has caused us losses in the billions. Yet we stand upright because of the trust invested in us by the people of this country. Had Mr. Khan been sincere he would have used the dharna to drawattention to our plight rather than attack us. Instead his government in KPK has stopped all advertising to our Group.

This spiteful behavior is a harbinger of the Naya Pakistan hewants to usher in, the spokesperson said. We have replied to his allegationsmany a timewhich you can read at: www.geo.tv/response.

By concluding we say with great emphasis that if anything we have said is wrong, Mr. Khan is free to challenge us and select a mutually acceptable arbitrator to resolve our differences.

Obsessive-Compulsive Disorder

Jon E Grant, J.D., M.D., M.P.H.

N Engl J Med 2014: 371:646-653 / August 14, 2014 / DOI: 10.1056/NEJMcp 1402176

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A 19-year-old man is brought to his primary physician by his father, who explains that his son washes his hands a hundred times a day, will not touch anything that has been touched by someone else without scrubbing it first, and has a fear of germs that has left him isolated in his bedroom, unable to eat, and wishing he were dead. Although the father reports that his son has always been finicky, this problem started approximately 2 years ago and has gradually become completely disabling. How should this patient be evaluated and treated?

THE CLINICAL PROBLEM

Obsessive–compulsive disorder (OCD) is a neuropsychiatric disorder characterized by obsessions or compulsions (or both) that are distressing, time-consuming, or substantially impairing. OCD is the fourth most common psychiatric illness, with a lifetime prevalence of 1 to 3%.[1,2] The World Health Organization has identified OCD as a leading global cause of nonfatal illness.[3]

KEY CLINICAL POINTS

Obsessive–Compulsive Disorder

Obsessive–compulsive disorder (OCD) is a common, disabling psychiatric disorder characterized by intrusive and unwanted thoughts, images, or urges that cause distress or anxiety and repetitive thoughts or actions that the person feels driven to perform.

OCD is commonly misdiagnosed as anxiety or depression, and an accurate diagnosis is important for appropriate therapy.

Only approximately one third of patients with OCD receive appropriate pharmacotherapy, and fewer than 10% receive evidence-based psychotherapy.

First-line therapies for OCD include exposure and response prevention, which uses repeated and prolonged exposures to fear-eliciting stimuli, combined with strict abstinence from compulsive behaviors, and selective serotonin-reuptake inhibitors, which are often used at higher doses in OCD than in depression or anxiety.

The hallmark of OCD is the presence of obsessions, compulsions, or both (Table 1TABLE 1  Criteria for the Diagnosis of Obsessive–Compulsive Disorder (OCD).).[4] Obsessions are repetitive and persistent thoughts (e.g., of contamination), images (e.g., of violent scenes), or urges (e.g., to stab someone). Obsessions are intrusive, unwanted thoughts that cause distress or anxiety. The person attempts to ignore or suppress these obsessions with another thought or action (i.e., a compulsion). Compulsions (or rituals) are repetitive behaviors (e.g., washing) or mental acts (e.g., counting) that the person feels driven to perform in response to an obsession. Compulsions are meant to neutralize or reduce the person's discomfort or to prevent a dreaded event.

Everyone obsesses about some event occasionally. The diagnosis of OCD, however, generally requires that obsessive thoughts occur for more than 1 hour each day. In addition, obsessions related to OCD do not suddenly start and stop with a specific event. Although many people know about obsessions regarding contamination, there are many variations of OCD (Table 2TABLE 2  Common Symptoms in OCD.), and patients often do not realize that certain thoughts they have are consistent with OCD. Most persons with OCD have multiple obsessions and compulsions. Although the themes underlying OCD (e.g., abnormal risk assessment such that the most improbable outcome is considered almost certain) appear to be similar across cultures,[5] cultural factors may influence the content of obsessions (e.g., a predominance of aggressive and religious obsessions has been reported in studies conducted in Brazil and Middle Eastern countries).[6] In addition, subtypes of OCD appear to vary according to age or developmental

stage of the patient (e.g., rates of harm obsessions, such as fears of death or illness regarding oneself or loved ones, are higher among children and adolescents than among adults).[7]

Among adults with OCD, the sex ratio is approximately 1:1.[2] The age at the onset of OCD appears to be bimodal, with onset either during childhood (mean age at onset, approximately 10 years) or during adolescence or young adulthood (mean age at onset, approximately 21 years).[8] Onset is earlier in boys than in girls,[9] and onset after 30 years of age is unusual.[10] In childhood-onset OCD, boys are more commonly affected than girls (male:female ratio, 2:1 to 3:1), whereas the sex ratio shifts among persons with onset during or after puberty (male:female ratio, 1:1.4).[11]

The cause of OCD remains poorly understood. Childhood-onset OCD is estimated to be 45 to 65% heritable, and OCD with an onset during adolescence or adulthood 27 to 47% heritable.[12] Although genomewide association studies have suggested candidate genes, findings have been inconsistent and many have not been replicated or withstood rigid statistical analysis.[13,14]

Several brain structures and functions have been implicated in OCD. Studies have consistently shown hyperactivity in the orbitofrontal cortex and caudate.[15,16] Other key implicated regions (suggesting abnormalities in functional or structural connections) include the anterior cingulate cortex, thalamus, amygdala, and parietal cortex.[17-19] Neuropsychological studies involving patients with OCD have shown deficits in cognitive abilities that are linked to the functioning of the frontal lobe and its related frontosubcortical structures, such as executive functioning, impulsivity in motor function, and cognitive inflexibility (i.e., not changing behavior on the basis of new information).[20,21]

If OCD is untreated, the course is usually chronic, often with waxing and waning symptoms. Without treatment, remission rates among adults are low (approximately 20%).[22] With appropriate treatment, patients report substantially higher rates of symptom response and remission.[23] Higher rates of symptom remission among treated patients, as compared with untreated patients, have been associated with a shorter duration of illness,[24] suggesting that early diagnosis and treatment may lead to improved outcomes. However, only approximately one third of patients with OCD receive appropriate pharmacotherapy, and fewer than 10% receive evidence-based psychotherapy.[25]

STRATEGIES AND EVIDENCE

Diagnosis

The diagnostic criteria for OCD are reviewed in Table 1. OCD is often misdiagnosed as anxiety or depression, and these and other conditions may also be misdiagnosed as OCD (Table 3TABLE 3  Conditions That May Be Misdiagnosed as OCD.). Patients who meet the criteria for OCD should be assessed with regard to their conviction that their obsessive beliefs are accurate. Poor insight, to varying degrees, occurs in 14 to 31% of persons with OCD and has been associated with worse treatment outcomes.26 In addition, up to 30% of persons with OCD have a tic disorder, the presence of which has been associated with a poor response to pharmacotherapy for OCD in children and adolescents.27

Management

Psychotherapy

Multiple types of psychotherapy have been examined in the treatment of OCD. Evidence from randomized trials, however, strongly supports the use of exposure-and-response-prevention therapy or cognitive therapy for OCD.

Exposure-and-Response-Prevention Therapy

Exposure and response prevention consists of repeated and prolonged exposures to fear-eliciting stimuli or situations, combined with instructions for strict abstinence from compulsive behaviors. Fear-eliciting stimuli or situations are presented in a hierarchical manner, beginning with moderately distressing ones and progressing to more distressing cues. The therapist then instructs the patient to abstain from the compulsive behavior that the patient believes will prevent the feared outcome or reduce the distress (e.g., washing hands after touching the toilet handle). The purpose of these exercises is to allow the patient to experience a reduction of the fear response, to recognize that these situations are not high risk, and to learn that anxiety will subside naturally if the patient does not make efforts to avoid it.

Patients are instructed to focus directly on aspects of the feared situation that increase anxiety and obsessive thoughts, and they may need to be reminded to do so during the exposure because many will engage in subtle avoidance or distraction. For exposures to be maximally effective, patients must persist with them until they learn that anxiety will reduce naturally. Patients are typically instructed to complete the exposure daily and to keep a record of their anxiety and discomfort ratings and the frequency and duration of exposure completion. Randomized trials assessing adherence to therapy have shown that complete response prevention during exposure therapy yields outcomes superior to those associated with partial or no response prevention.[28,29]

Analyses of more than two dozen randomized, controlled trials have shown that approximately 60 to 85% of patients report a considerable reduction in symptoms with the use of exposure and response prevention, and improvement is maintained for up to 5 years after the discontinuation of treatment in a majority of the patients who have a response to therapy.[30,31] Exposure-and-response-prevention therapy can be delivered in multiple formats, including by telephone[32] or by computer or Internet with minimal therapist support,[33,34] with similar efficacy. In addition, data from a randomized trial indicated that self-guided exposure for OCD, with the use of standardized materials, has a level of effectiveness that is similar to therapist-supervised exposure.[35]

On the basis of data from randomized trials, exposure therapy should be delivered weekly or twice weekly, for approximately 20 to 30 total hours of therapy. After the short-term treatment, exposure therapy should be delivered as monthly "booster" sessions for 3 to 6 months to maintain gains.

Cognitive Therapy

Unwanted, intrusive thoughts are a common experience in the general population.[36] Distressing and time-consuming obsessions arise when these otherwise normal, intrusive thoughts are appraised as highly meaningful and as posing a threat for which the patient is personally responsible. The person then becomes preoccupied with the unwanted thought and with trying to control it. Cognitive therapy for OCD focuses on teaching patients to identify and correct their dysfunctional belief about feared situations. Cognitive therapy assists patients in reducing anxiety and compulsions by identifying these automatic unrealistic thoughts and changing their interpretations.

When undergoing cognitive therapy, the patient keeps a daily diary of obsessions and interpretations associated with the obsessions. Using Socratic questioning, the therapist challenges the unrealistic belief and helps the patient identify the cognitive distortion.

The therapist implements behavioral experiments (e.g., a patient is asked to touch a range of dirty objects without washing the hands and to keep a log of how often illness follows after doing so) to disprove errors in thinking about cause and effect. Behavioral experiments used in cognitive therapy differ from the exercises used in exposure-and-response-prevention therapy in that, while engaging in the feared behavior, patients are not focusing on anxiety reduction (as with exposure and response prevention) but instead are challenging the belief that they could ultimately become ill by not washing. Patients thereby learn to identify and reevaluate beliefs about the potential consequences of engaging in or refraining from compulsive behaviors.

In randomized, controlled trials, cognitive therapy has shown improvement in 60 to 80% of patients, with effect sizes almost as large as those with exposure and response prevention. As with exposure and response prevention, however, dropping out of cognitive therapy prematurely is common (20 to 30% of patients).28 Although cognitive therapy may be a viable alternative for patients who are reluctant to participate in exposure and response prevention, exposure therapy is supported by a larger body of empirical data and is therefore recommended as the first-line psychotherapy treatment for OCD.37,38

Pharmacotherapy

In addition to exposure and response prevention, pharmacotherapy with the tricyclic antidepressant clomipramine or a selective serotonin-reuptake inhibitor (SSRI; paroxetine, fluvoxamine, fluoxetine, citalopram, escitalopram, and sertraline) has shown efficacy in OCD.39 (Table 4TABLE

4 Medications Approved by the Food and Drug Administration (FDA) for the Treatment of OCD.). A meta-analysis of 17 randomized, double-blind, placebo-controlled trials (generally short-term; i.e., 8 to 12 weeks) that studied various SSRIs showed that all were superior

to placebo and that patients were approximately twice as likely to have a response to an SSRI than to placebo.[40] A meta-analysis of 7 controlled trials of clomipramine also showed that this medication was superior to placebo.[41] Although data are limited, comparisons between different SSRIs or between an SSRI and clomipramine have shown no significant differences in efficacy. The SSRIs are recommended as first-line pharmacologic treatment for OCD (over clomipramine) owing to their better adverse-event profile.[42] When used for OCD, as compared with other disorders such as depression or generalized anxiety, SSRIs tend to take longer to be effective (between 4 and 12 weeks), and higher doses are often required.[42]

Approximately 40 to 65% of patients with OCD have a response to an SSRI or clomipramine, with a mean improvement in the severity of symptoms of approximately 20 to 40%.[23,43] The probability of full remission of OCD with the use of pharmacotherapy alone is low (11% of patients in one study).[43] An early age at OCD onset, more severe OCD, coexisting tics, and hoarding symptoms have all been associated with a poor response to clomipramine and SSRIs.[42]

For patients who have a response to pharmacotherapy, treatment is generally continued for 1 to 2 years, followed by gradual tapering of the medication. Although limited data support the 2-year recommended period of medication, 25 to 40% of patients have a relapse if they discontinue medication after 2 years, whereas treatment with medication for shorter periods of time has resulted in relapse rates of up to 80% after the discontinuation of medication.[44] When relapse occurs, medications are generally restarted and continued indefinitely.

Comparison of Treatments and Combination Therapies

A meta-analysis of nine short-term trials (generally 8 to 12 weeks) comparing exposure and response prevention with pharmacotherapy showed a greater benefit overall with exposure therapy. In stratified analyses, the differences were significant in trials involving children but not in those involving adults.[45] The use of exposure therapy in combination with medication has resulted in outcomes superior to those with medication alone but not to outcomes with exposure therapy alone.[45]

Results from a limited number of small and short-term (4 to 12 weeks), double-blind, placebo-controlled trials support a benefit to adding other medications (some second-generation antipsychotic agents, stimulants, or glutamate modulators) when there is a partial initial response to SSRIs.[46,47] However, none of these augmentation medications have been approved by the Food and Drug Administration (FDA) for this purpose, and more data are needed.

Choice of Initial Therapy

Guidelines from the American Psychiatric Association recommend exposure and response prevention as monotherapy for persons who are motivated to cooperate with the demands of the therapy, who do not have severe depressive symptoms, or who prefer not to take medication.[42] In the case of patients who find exposure therapy too frightening, an SSRI should be started first, and then exposure therapy initiated after the medication has reduced the OCD symptoms, if the patient is then agreeable to this therapy.

Use of an SSRI as monotherapy is recommended for persons who are not able to engage in exposure therapy, who report a previous response to an SSRI, or who prefer medication over psychotherapy. A combination of an SSRI and exposure therapy is recommended for persons who have other coexisting conditions that could benefit from medication treatment (e.g., major depression) or who have an unsatisfactory response to either monotherapeutic approach. Combined treatment is also recommended for persons who prefer to take medication for the shortest possible time, because data from uncontrolled follow-up studies suggest that exposure therapy may help to prevent or delay relapse when the SSRI is discontinued.[48]

Deep-Brain Stimulation

Deep-brain stimulation or ablative neurosurgery (e.g., capsulotomy and cingulotomy) may be considered in patients with severe, incapacitating OCD that has not had a response to an adequate number of sessions of exposure therapy, two or more adequate trials of SSRIs, a trial of clomipramine, and at least three trials of an augmentation therapy. Only a very small minority of patients with OCD qualify for such treatment. Although several centers worldwide offer ablative surgery as a last-resort option for severe OCD, only deep-brain stimulation (specifically, of the

ventral capsule or ventral striatum) has been approved by the FDA for the treatment of OCD. In double-blind trials comparing stimulation with sham stimulation, response rates have been approximately 50 to 60% with stimulation, as compared with approximately 10% in the off or sham condition.[49] The data for deep-brain stimulation, however, derive from a small number of studies involving few patients. The literature on deep-brain stimulation for OCD generally reports a low rate of serious adverse events related to surgery or device malfunction. Intracerebral brain hemorrhage, postoperative confusion, which is usually transient but may persist, and device-related infection, however, are all risks associated with the surgery.[49]

AREAS OF UNCERTAINTY

Trials of medication for OCD have been largely short-term and have involved predominantly young or middle-aged adults. Data are lacking to inform long-term benefit and risks and to inform use in children and elderly persons with OCD. More research is also needed to identify the predictors of poor outcomes.

Although exposure therapy has shown a benefit in the treatment of OCD, little is known about how well the therapy is performed in the community. The genetic factors predisposing persons to OCD remain incompletely understood. A better understanding is needed with regard to childhood risk factors for OCD and how these variables interact with genetic factors. Such information may allow for the identification of children at risk for OCD and the development of early-intervention strategies. Clinical trials have largely focused on treatment of the core symptoms of OCD, but effective treatments are also needed for associated social dysfunction.

GUIDELINES

The American Psychiatric Association (United States) and the National Institute for Health and Care Excellence (United Kingdom) have published guidelines regarding the diagnosis and management of OCD.[42,50] The recommendations in this article are consistent with these guidelines.

CONCLUSIONS AND RECOMMENDATIONS

The man described in the vignette has a classic case of contamination OCD. He should be questioned regarding other possible obsessions and compulsive behaviors. Assessments regarding his level of insight and the presence of a tic disorder are relevant to assessing prognosis and the choice of therapy.

Once the diagnosis is made, the clinician should educate the patient about the nature of the illness, including the low frequency of spontaneous improvement but the high likelihood of responsiveness to therapy. The patient should be informed that exposure-and-response-prevention therapy and pharmacotherapy with an SSRI are considered to be first-line treatments that improve OCD symptoms in a majority of patients. To help the patient choose his treatment, he should be educated regarding the process of exposure therapy and the probable length of treatment (weekly sessions for approximately 16 weeks, followed by some monthly sessions). Similarly, he should be educated regarding medication side effects and told that medication ought to be continued for at least 1 year.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

SOURCE INFORMATION

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Caffeinated 'energy' drinks bad for heart

London: "Energy" drinks which are so popular during physical exercise and even otherwise among children and younger adults can cause heart problems, a research shows.

"People sometimes consume a number of these drinks one after the other. This situation can lead to a number of adverse conditions, including angina, cardiac arrhythmia (irregular heartbeat) and even sudden death," warned professor Milou-Daniel Drici from France.

Speaking at the European Society of Cardiology (ESC) Congress, 2014, in Barcelona, Spain, he said that around 96 per cent of these drinks contain caffeine, with a typical 0.25 litre holding as much as two espressos worth of caffeine.

"We found that caffeine syndrome was the most common problem. It is characterised by a fast heart rate (called tachycardia), tremor, anxiety and headache," he informed.

Caffeine is one of the most potent agonists - a chemical that binds to a receptor and activates the receptor to produce a biological response - of the ryanodine receptors and leads to a massive release of calcium within cardiac cells.

This can cause arrhythmias but also has effects on the heart's abilities to contract and to use oxygen.

The current study analysed adverse events reported to A.N.S.E.S - the French agency for food safety.

The researchers found that consumption of the 103 energy drinks in France increased by 30 per cent between 2009 and 2011 up to over 30 million litres.

"Doctors should warn patients with cardiac conditions about the potential dangers of these drinks and ask young people in particular whether they consume such drinks on a regular basis or binge drink," Dr Drici concluded.

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PIMA, FIMA doctors, relief supplies stopped at Gaza border

By M. Waqar Bhatti

From an article in the News

A number of Pakistani specialists and the medical supplies intended for Palestinians have been stopped by Egyptian and Israeli authorities at the Gaza border.

"Many trauma surgeons, orthopaedics, paediatricians, psychologists and anaesthetics had volunteered to go to Gaza but the Egyptian and Israeli governments are not allowing them to go inside the besieged area," Pakistan Islamic Medical Association (Pima) President Dr Sohail Akhtar told The News on Thursday.

The Gaza health ministry had appealed to the Federation of Islamic Medical Associations (Fima) to provide 20 ambulances, medical supplies, health equipment and specialists after over 9,000 people were injured besides the 1,900 killed in a month-long brutal Israeli assault in Gaza.

Pima arranged four ambulances as well as medical supplies worth millions of rupees to provide medical assistance to thousands of wounded Palestinians.

Pima currently leads Fima, an alliance of 35 international medical associations of the world. Pima's Dr Tanveer Zubairi is the Fima chairman.

"Fima has [also] arranged 20 state-of-the-art ambulances, which are ready to be shifted to Gaza at Egypt's Rafah border crossing, but Israel has let only four of them to go into Gaza," he said. "Medical supplies for thousands of patients are also awaiting permission at the Cairo airport to be transported into Gaza."

So far Israel has let three convoys of medical supplies, two from Fima and one from Doctors Worldwide, inside Gaza. Only 13 doctors, including eight Sudanese specialists and five Arabs, have been allowed to enter the Gaza strip to assist local doctors. Hundreds of doctors from all over the world, including United States and Pakistan, are awaiting permission to help the wounded Palestinians

"In the last few weeks, dozens of Pakistani specialists have contacted PIMA and expressed their willingness to go to Gaza," Akhtar added.

"The Israeli government has told Fima it would allow ambulances into Gaza on their conditions," the Pima president claimed. "First, the ambulances should be bought from Israel which they are selling on exorbitant rates. Second, the ambulances should be given to people nominated by Israel, to which Fima has refused."

Five WHO health kits, each enough for medical needs of 50,000 people, are also stranded in Egypt, according to him.

Fima, he said, has decided to either construct a hospital in Gaza to treat the wounded or to reconstruct one of the health facilities destroyed in the shelling by Israeli forces.

Around 12 hospitals and 5 primary healthcare facilities were destroyed by Israel, killing patients and doctors inside them and worsening the healthcare system in the besieged territory.

Akhtar said Pakistani doctors as well as people were donating generously for the Palestinians and the fund-raising campaign would continue without any break.

He also appealed to government to use its influence on the Egyptian government to let medical supplies, medicines, equipment and health experts into Gaza from the Rafah border so that thousands of lives could be saved.

Witch hunt against Israel's war critics

'Israeli pilots perpetrated the cruelest and most despicable deeds against Gaza's weakest and most helpless'

In Israel, dissent against the war in Gaza is bitterly quashed. The few who speak out complain of being harassed, intimidated or even sacked. The once mighty left has disappeared.

It has been Israel's deadliest conflict in years. More than 1,960 Palestinians were killed and 64 Israeli soldiers died fighting what some see as an unwinnable war.

And yet the only significant protest in Israel so far saw thousands late on Thursday demand an end to Hamas rocket attacks, dissatisfied with the status quo after ground troops pulled out and a ceasefire was extended.

Liberal newspaper Haaretz decried on Friday what it called a "witch hunt" against leftists and civil rights organisations after the director of the national service administration, Sar-Shalom Jerbi, told rights group B'Tselem it was being blacklisted as an employer.

"I feel obligated to exercise my power and stop the state assistance provided to an organisation that works against the state and against soldiers who are heroically giving their very lives to protect the safety and well-being of all citizens," Jerbi wrote in a letter.

He accused B'Tselem of disseminating lies and slander, endangering the state and publishing information that encourages Israel's enemies and leads to violent anti-Semitic acts against Jews around the world.

The rights group denounced the move as an attack on Israeli democracy, and asked supporters to sign an online petition to support freedom of expression and democracy.

Yizhar Beer of the Keshev Centre for the Protection of Democracy in Israel says it has never been more difficult to voice dissent in a country which prides itself on being the only democracy in the Middle East.

Israeli public opinion has overwhelmingly supported the war. A poll carried out by The Israel Democracy Institute last month said 95 percent of Israeli Jews believed the offensive was just. In a country with compulsory national conscription, almost everybody has a friend or relative in the army. Hamas rocket attacks have tormented millions of Israelis, inflicting fear and panic in border communities, regardless of the fact that hundreds are shot down and just three civilians have been killed since July.

In Israel, as in most countries during time of war, the local media have been patriotic champions of the offensive, uniting behind their boys on the frontline, sending them presents, highlighting the suffering of Israeli citizens and downplaying suffering on the other side.

The few who have spoken out of line have been threatened or denounced as traitors.

After Haaretz commentator Gideon Levy accused air force pilots of perpetrating "the cruelest and most despicable deeds" against Gaza's "weakest and most helpless," his employer hired him bodyguards.

Readers cancelled their subscriptions, people stopped in the street to insult him and government whip Yariv Levin denounced him as a liar, a "mouthpiece of the enemy" who should be put on trial for treason.

"I have never faced such aggressive reaction, never," Levy told AFP in his cramped office at Haaretz in Tel Aviv, away from the coffee shops where he fears being insulted.

"Nobody cares here about the suffering of Gaza. More than this, if you dare to express empathy you are a traitor," he said.

MQM Rabita Committee leaders removed, reinstated within hours

A few hours after a notification was issued on Sunday for their removal, the Muttahida Qaumi Movement's Coordination Committee retracted its orders and announced the reinstatement of Engineer Nasir Jamal and Dr Sagheer Ahmed to their positions.

Both senior leaders had been relieved of their duties with the committee in view of their increasing personal and official responsibilities. However, the committee later issued a statement to reinstate Jamal as the deputy convener, while also requesting him to continue his work with the party's central information and news committees.

Dr Ahmed was also advised to continue serving as the provincial health minister and make all possible efforts to bring about improvements that would facilitate Sindh's people.

(The News)

International Urdu conference to begin on October 16

By Sheher Bano

Karachi

In order to promote Urdu language and literature, the 7th International Urdu Conference would be held at the Arts Council from October 16 to 19.

Muhammad Ahmed Shah, the secretary of the Arts Council of Pakistan, announced this at a press conference on Friday. Arts Council President Ejaz Ahmed Farooqui was also present on the occasion.

He said initiated in 2008 by the Arts Council Karachi, Urdu conference was a regular annual feature eagerly awaited by the literary enthusiasts and cultural figures of the city.

“Beside the regular practice of presenting papers on Urdu language and literature, this time the conference will also include sessions on Urdu’s historic relation with other languages, Pakistani art, media, theatre, film etc,” he said.

Moreover, bilingual sessions in Urdu and English will also be held for the youth, along with a special session with the scholars and critics in which suggestions will be sought from them on ways

to bring peace in the region, the secretary said, adding a grand Aalmi Mushaira will also be a part of the conference.

Ahmed Shah said that veteran writers, critics, poets and scholars from around the world were participating in the conference. Mentioning some names, he said that besides the well-known poet, lyricist and scriptwriter Javed Akhtar, Javed Siddiqui, a great name in film and theatre arts, Dr Shamim Hanafi, Qazi Afzal Hussain, Sukhbir Singh Shaad, Shamsul Haq Usmani, Ubaid Siddqui and Farhat Ihsaas were coming from India. While Raza Ali Abidi from England, Ashfaq Hussain from Canada, Christina Osterheld from Germany, Khalil Toqar from Heidelberg, Turkey, Mohammad Ibrahim Al-Misri from Egypt, Dr Kulsoom and Abul Bashar from Bangladesh. Nasar Malik and Asad Malik from Norway, Lyudmila from Russia and others were coming specially to grace this conference.

Veteran writers and scholars, including Dr Mubarak Ali, Intizar Hussain, Abdullah Hussain, Amjad Islam Amjad, Asghar Nadeem Syed, Masood Ashar, Mustansar Hussain Tarar were also expected to attend the conference.

This year, as a first step, veterans from the fields of literature, music, theatre and others will get the life achievement awards. Ghazal maestro Mehdi Hasan will also be awarded posthumously.

Israel has received over $121 bn US aid since 1949

LAHORE: Having killed over 1,500 unarmed Palestinians during the last 26 days, Israel has received over $121 billion in non-inflation-adjusted bilateral assistance from the United States of America between 1949 and April 2014, reveals a recent report prepared by the American Congressional Research Service.

According to the April 11, 2014 report prepared for Members and Committees of the US Congress by Jeremy Sharp, a specialist in Middle Eastern Affairs, this figure of $121 billion thus makes Israel the largest cumulative global recipient of US foreign assistance since World War II.

In his report, Jeremy Sharp had stated: "Almost all US bilateral aid to Israel is in the form of military assistance, although in the past Israel had also received significant economic assistance. Strong congressional support for Israel has resulted in Israel receiving benefits not available to any other countries; for example, Israel can use some US military assistance both for research and development in the United States and for military purchases from Israeli manufacturers."

He had further asserted: "In addition, US assistance earmarked for Israel is generally delivered in the first 30 days of the fiscal year, while most other recipients normally receive aid in installments, and Israel (as is also the case with Egypt) is permitted to use cash flow financing for its US arms purchase."

According to Israel's oldest newspaper "The Haaretz," this nominal aid figure of $121 billion is actually equivalent to over $233.7 billion, if it is adjusting for inflation.Founded in 1918 and published both in Hebrew and English languages, "The Haaretz" had also quoted a 2013 statement aired by Moshe Arens, a former Israeli Foreign Minister, Defense Minister and the country's ambassador to Washington DC, which had clearly spelt out the fact that Israel happened to be the largest single recipient of American foreign aid.

Interestingly, just a fortnight ago on July 15, 2014, the United States Senate had shown its strong "love and affection" for Israel by approving an increase in its financial aid to the recipient nation's Iron Dome anti-missile system.

The US Senate Appropriations Defence subcommittee had agreed to allocate $351 million to finance the Israeli anti-missile system during fiscal year 2015 beginning on October 1, compared to $235 million in 2014.

Interestingly, the incumbent US President Barack Obama had requested only $179 million to support the system in 2015.A research conducted by "The News International" by taking into account some similar articles and news stories appearing in various prestigious American media outlets also reveal that US aid relationship with Israel is unlike with any other in the world.

The first US aid to Israel had arrived in 1949 and was used for such basic purposes as buying food and absorbing Jewish refugees. It began to expand a decade later with the first military aid. It grew gradually from a base of $100 million (in nominal terms) in 1949, before taking off after the Yom Kippur War and the signing of the Camp David agreements.

Since then, US aid has been about $3 billion annually, of which $1.8 billion is military assistance with the rest for civilian purposes. In 1998 Benjamin Netanyahu, in his first term as Israeli Prime Minister, had led a drive to convert the civilian portion to military aid, totaling $2.5 billion to $3 billion a year.

Israel had gone on to receive the most aid in the 1970s between the 1973 Yom Kippur War and the 1979 peace agreement with Egypt. For signing the accord with Egypt, Israel received its largest-ever amount of aid some $15.7 billion in grants and loans after adjusting for inflation (it was $4.7 billion at the time), which was used to fund the transfer of army bases in the Sinai Peninsula back into Israel.

The extent of American "generosity" towards Israel can also be gauged from the fact that the year 1974 had seen particularly high level of American assistance flowing to Israel.This was the year when the United States had helped Israel reestablish its military standing after the losses it suffered in the Yom Kippur War.

In inflation-adjusted terms, Israel received $12.4 billion ($2.6 billion in nominal terms) during 1974. In 1976, Israel had received another $9.6 billion ($2.3 billion in nominal terms).

The above-mentioned numbers and statistics do not include loan guarantees amounting to about $19 billion that Washington has granted Israel in recent years to make it easier for it to borrow overseas. It also doesn't include the transfer of surplus military equipment to Israel.

Research further shows that between 1974 and 1989, some $16.4 billion in the American military loans to Israel were converted to grants and that this was the understanding from the very beginning.

Indeed, a good amount of the past US loans to Israel were eventually forgiven by the Congress, which has undoubtedly helped Israel's often-touted claim that they have never defaulted on any American government loan!

Diagnosis of Obstructive Sleep Apnea in Adults: A Clinical Practice Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA;

Ann Intern Med. 2014;161(3):210-220. doi:10.7326/M12-3187

http://annals.org./article.aspx?articleid=1892620

Description: The American College of Physicians (ACP) developed this guideline to present the evidence and provide clinical recommendations on the diagnosis of obstructive sleep apnea in adults.

Methods: This guideline is based on published literature on this topic that was identified by using MEDLINE (1966 through May 2013), the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews. Searches were limited to English-language publications. The clinical outcomes evaluated for this guideline included all-cause mortality, cardiovascular mortality, nonfatal cardiovascular disease, stroke, hypertension, type 2 diabetes, postsurgical outcomes, and quality of life. Sensitivities, specificities, and likelihood ratios were also assessed as outcomes of diagnostic tests. This guideline grades the evidence and recommendations by using ACP's clinical practice guidelines grading system.

Recommendation 1: ACP recommends a sleep study for patients with unexplained daytime sleepiness. (Grade: weak recommendation, low-quality evidence)

Recommendation 2: ACP recommends polysomnography for diagnostic testing in patients suspected of obstructive sleep apnea. ACP recommends portable sleep monitors in patients without serious comorbidities as an alternative to polysomnography when polysomnography is not available for diagnostic testing. (Grade: weak recommendation, moderate-quality evidence)

Obstructive sleep apnea (OSA) is caused by repetitive obstruction of the upper airway during sleep, resulting in hypopnea (reduced airflow during sleep) or apnea (complete airflow cessation during sleep). Persons with OSA may experience loud snoring, oxygen desaturation, frequent arousals, and disruption of sleep. Disrupted sleep can result in hypersomnolence and impaired concentration during the day, increased probability of motor vehicle and other accidents, and decreased quality of life. Although evidence establishing a causal relationship is not currently available, OSA is

associated with adverse clinical outcomes, including cardiovascular disease; hypertension; cognitive impairment and metabolic abnormalities, such as type 2 diabetes ; and an increased risk for postoperative cardiac and respiratory complications. The exact prevalence of OSA is unknown. Estimates range from 10% to 17% of the U.S. population, with the variation due in part to variable criteria used to define disease (for example, the number of apneic episodes per hour or whether individuals are required to have specific accompanying signs or symptoms). Prevalence of OSA increases with age, particularly in adults older than 60 years. The growing rate of obesity also contributes to increasing OSA prevalence.

Considerable controversy surrounds the type and level of respiratory abnormality, the presence and type of signs or symptoms, and the most appropriate sleep monitoring device for diagnosing OSA. Questionnaires are used to prescreen patients for further testing, the most common of which is the Epworth Sleepiness Scale (ESS). Polysomnography (PSG), which must be performed in a sleep laboratory setting, is considered the reference standard for diagnosing OSA, but it is expensive and requires specialized resources. Type I monitors are facility-based PSG. Type II monitors are portable, measure most of the same channels (physiologic parameters) as type I monitors (including ≥2 respiratory channels), and can differentiate between sleep and awake states. Type III monitors also measure at least 2 respiratory channels but cannot reliably distinguish between sleep and awake states. Type IV monitors are those that do not fit into type III classification and can vary in the number of channels that they record. Table 1summarizes the types of monitors.

Table 1. Types of Monitors for Diagnosis of Obstructive Sleep Apnea*

Table 1. **Types of Monitors for Diagnosis of Obstructive Sleep Apnea***

Type	Portability	Channels, *n*	Signals	≥2 Airflow/Effort Channels	Identifies Sleep and Awake States	Measures AHI
I	Facility-based	14–16	EEG, EOG, EMG, ECG/HR, airflow, effort SaO_2	Yes	Yes	Yes
II	Portable	≥7	EEG, EOG, EMG, ECG/HR, airflow, effort SaO_2	Yes	Yes	Yes
III	Portable	≥4	Airflow and/or effort, ECG/HR, SaO_2	Yes	No	No, but estimates AHI†
IV	Portable	1–3‡	All monitors that do not fit into type III classification	No	No§	No, but estimates AHI†

AHI = apnea–hypopnea index; ECG = electrocardiography; EEG = electroencephalography; EMG = electromyography; EOG = electro-oculography; HR = heart rate.
* Adapted from reference 28.
† Both type III and type IV monitors estimate the AHI by measuring the total number of episodes of apnea and hypopnea divided by the number of recording hours/time (as opposed to number of hours of sleep determined by EEG). Some type IV devices estimate sleep and awake states by peripheral arterial tone and estimate the AHI from the estimated sleep time.
‡ May have >3 channels provided that criteria for type III monitors are not met.
§ May include monitors that measure signals that are, in principle, able to identify arousals from sleep.

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Polysomnography and portable monitors measure or estimate the apnea–hypopnea index (AHI), a measure of the number of apnea or hypopnea events per hour during sleep (Table 1). The AHI is

used to diagnose and assess the severity of OSA. The American Academy of Sleep Medicine (AASM) sets a threshold of 15 events per hour with or without symptoms or 5 events per hour with symptoms for OSA diagnosis. The Centers for Medicare & Medicaid Services reimburses for OSA treatment with continuous positive airway pressure (CPAP) devices for patients with an AHI score of at least 15 events per hour or those with at least 5 events per hour and symptoms, such as daytime somnolence, fatigue, insomnia, mood disorders, and cognitive impairment, or cardiovascular comorbid conditions, such as hypertension, ischemic heart disease, or prior stroke.

The purpose of this American College of Physicians (ACP) guideline is to address the screening and diagnosis of OSA by presenting a comparison of the effectiveness of the available diagnostic methods. The target audience for this guideline includes all clinicians, and the target patient population includes all adults with suspected OSA. This guideline is based on the comparative effectiveness review sponsored by the Agency for Healthcare Research and Quality (AHRQ), the 2007 Technology Assessment of Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome, and an updated literature review through May 2013. The recently published ACP guideline on the management of OSA in adults provides guidance on treatment of OSA.

This guideline addresses the following key questions related to the screening and diagnosis of OSA:

1. How do different available tests compare in their ability to diagnose sleep apnea in adults with symptoms suggestive of disordered sleep? How do these tests compare in different subgroups of patients based on race, sex, body mass index, existing type 2 diabetes mellitus, existing cardiovascular disease, existing hypertension, clinical symptoms, previous stroke, or airway characteristics?
2. How does phased testing (screening tests or battery followed by full test) compare with full testing alone?
3. What is the effect of preoperative screening for sleep apnea on surgical outcomes?
4. In adults being screened for OSA, what is the relationship between the AHI and other patient characteristics with respect to long-term clinical and functional outcomes?

The literature search for the systematic review was conducted using MEDLINE (1966 to September 2010), the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews and included peer-reviewed studies published in English. The evidence review was updated through 30 May 2013 by identifying literature in MEDLINE with the same search strategy and inclusion and exclusion criteria as the 2010 report (Supplement). The included studies reported minimum AHI thresholds for OSA diagnosis ranging from 5 to 20 events per hour. Further details about the methods and inclusion and exclusion criteria applied in the evidence review are available in the AHRQ report and the Supplement.

This guideline rates the evidence and recommendations by using ACP's guideline grading system (Table 2). Details of the guideline development process can be found in ACP's methods paper.

Table 2. The American College of Physicians' Guideline Grading System*

Table 2. **The American College of Physicians' Guideline Grading System***

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

* Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) workgroup.

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Type II Monitors Versus PSG

Moderate-quality evidence from 9 studies showed that type II monitors may predict AHI scores suggestive of OSA. The sensitivities and specificities for type II monitors to predict AHI scores greater than 5, 15, and 30 events per hour are summarized in Table 3.

Table 3. Accuracy of Portable Monitors and Questionnaires for Diagnosis of Obstructive Sleep Apnea

Table 3. **Accuracy of Portable Monitors and Questionnaires for Diagnosis of Obstructive Sleep Apnea**

Tool	Overall Quality of Evidence	AHI Cutoff, *events/h*	Sensitivity, %	Specificity, %
Type II monitor	Moderate	5	88–94	36–77
		15	79–100	71–100
		30	61–77	96–98
Type III monitor	Moderate	5	83–97	48–100
		15	64–100	41–100
		30	70–96	79–100
Type IV monitor				
≥2 channels	Moderate	5	75–100	43–100
		15	67–98	50–100
		30	80–100	74–98
1 channel/oximetry	Moderate	5	27–100	67–100
		15	39–100	32–100
		30	18–100	29–100
Berlin Questionnaire	Low	5	37–93	17–95
		15	40–83	20–97
		30	17–87	37–77
Epworth Sleepiness Scale	Low	5	24–96	29–89
		15	21–50	43–83
		30	36–50	70–79
Multivariate Apnea Prediction Index	Low	5	84	46
		15	86	31
		30	90	66
Pittsburgh Sleep Quality Index	Low	5	72	0
		15	14	86
		30	No data	No data
STOP-BANG Questionnaire	Low	5	36–97	18–89
		15	44–99	11–77
		30	56–100	11–74

AHI = apnea–hypopnea index.

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Type III Monitors Versus PSG

Moderate-quality evidence from 34 studies showed that type III monitors have the ability to predict AHI scores suggestive of OSA. The sensitivities and specificities for type III monitors to predict AHI scores greater than 5, 15, and 30 events per hour are summarized in Table 3. Type III monitors showed a wide range of difference in AHI estimates compared with PSG.

Type IV Monitors Versus PSG

Moderate-quality evidence from 37 studies showed that type IV monitors can predict AHI scores suggestive of OSA. The sensitivities and specificities for type IV monitors to predict AHI scores greater than 5, 15, and 30 events per hour are summarized in Table 3. Type IV monitors showed a

wide range of difference in AHI estimates compared with PSG. Direct comparison between type III and type IV monitors was not possible, but indirect evidence from studies comparing each monitor with PSG suggested that type III monitors performed better than type IV monitors in predicting AHI scores suggestive of OSA.

Questionnaires Versus PSG

A total of 47 studies compared questionnaires and PSG. The sensitivities and specificities of selected tests are summarized in Table 3. Low-quality evidence from 18 studies showed that the Berlin Questionnaire may be helpful in predicting risk for OSA. However, the sensitivity and specificity of the questionnaire had a wide range depending on the AHI cutoff level (Table 3). Low-quality evidence from 22 studies describing the ESS, 3 describing the Multivariate Apnea Prediction Index, 3 describing the Pittsburgh Sleep Quality Index, and 5 describing the STOP-BANG Questionnaire showed that these questionnaires had low accuracy for diagnosis. Evidence was insufficient to determine the diagnostic accuracy of the other questionnaires.

Clinical Prediction Rules Versus PSG

Thirteen studies assessed a total of 16 internally validated clinical prediction rules (refer to the AHRQ report and the Supplement for descriptions of each of these tools). Most of the rules used information that was available through clinical history and examination, and all were compared with facility-based PSG. Studies were highly heterogeneous with respect to populations assessed, type of reference test used, and OSA definitions, and only 1 study was identified for each prediction rule. Overall, low-quality evidence suggested that some clinical prediction rules can be used to effectively predict OSA diagnosis. However, the applicability of these rules to the general population cannot be determined from the existing literature. In addition, none of the studies examined the potential clinical utility of applying these rules to clinical practice.

Comparison of Phased Testing Versus Full Testing

Phased testing involves a series of tests that may be done depending on the results of initial tests, whereas full testing involves overnight PSG. Evidence was insufficient to determine the utility of phased testing for diagnosing OSA; 1 low-quality prospective study was subject to verification bias, and another reported a positive likelihood ratio of at least 3.9 and a negative likelihood ratio of 0.06.

Fourteen studies met the inclusion criteria for predictors of long-term clinical outcomes, such as mortality, stroke, hypertension, and cardiovascular diseaseResults were inconclusive to establish a causal relationship and are summarized in Table 4.

Table 4. The AHI as a Predictor of Clinical Outcomes

Table 4. **The AHI as a Predictor of Clinical Outcomes**

Outcome	Evidence	Overall Quality of Evidence	Reference
All-cause mortality	Association with increased risk with AHI score >30 events/h	High	19, 20, 171, 172, 176
Cardiovascular mortality	Inconsistent results	Insufficient	5, 20
Nonfatal cardiovascular disease	Association with increased risk with AHI score ≥30 events/h and no CPAP treatment	Insufficient	5, 177
Stroke	No association	Insufficient	169
Hypertension	Unclear conclusions	Insufficient	10, 173, 178
Type 2 diabetes	Association with increased risk with AHI score >30 events/h	Low	170, 174
Quality of life	No association	Insufficient	175

AHI = apnea–hypopnea index; CPAP = continuous positive airway pressure.

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Polysomnography performed in a sleep laboratory has been the standard method to diagnose OSA; however, it requires specialized facilities, is resource-intensive and expensive, and requires patients to spend the night under observation in a foreign environment. In addition to PSG, portable monitors (types II, III, and IV) can be used to diagnose OSA, although the measured AHI score can differ substantially from that measured with PSG. Low-quality evidence showed that type II monitors may identify AHI scores suggestive of OSA. No study directly compared different portable monitors with each other, although current evidence supports greater diagnostic accuracy with type III monitors than type IV monitors (28). The utility of portable monitors for diagnosing OSA in patients with comorbid conditions, including chronic lung disease, congestive heart failure,

or neurologic disorders, is uncertain because most studies excluded these patients. Also, compared with PSG, type II, III, and IV monitors had a wide range of difference in AHI estimates.

A significant limitation of type IV monitors is that they cannot differentiate between obstructive and central apneas. In contrast to OSA, where airflow is disrupted because of airway obstruction, central sleep apnea results from a temporary failure of the brain to send signals to breathe. Because CPAP may be contraindicated in patients with central sleep apnea, an accurate diagnosis is important. Patients with cardiac, respiratory, or neurologic disease may be at the greatest risk for central sleep apnea, and the AASM does not recommend the use of portable monitors for diagnosis in these patients.

Although the evidence was insufficient to determine the utility of most questionnaires compared with PSG for OSA screening, low-quality evidence indicated that the Berlin Questionnaire may be used to screen for OSA. However, questionnaires may not be applicable to the general population because they include subjective questions about sleepiness and not all patients, even those with severe OSA, report sleepiness. For example, the Wisconsin Sleep Cohort Study found that only 37% of patients with severe OSA (AHI score ≥30 events/h) reported daytime sleepiness and that mortality associated with long-term OSA was independent of subjective sleepiness.

Evidence was insufficient to determine the effectiveness of phased testing for the diagnosis of OSA or the utility of preoperative screening for OSA to improve postsurgical outcomes.

Evidence was mixed to correlate OSA with predictors of long-term clinical outcomes, and no causal relationships have been established. High-quality evidence showed an association between an AHI score greater than 30 events per hour and greater all-cause mortality. Low-quality evidence showed an association between higher AHI score and incident diabetes, although obesity was probably a confounding variable in these studies. However, a randomized trial showed that CPAP treatment did not reduce mortality or coronary heart disease events in patients with OSA who did not have daytime sleepiness. Although CPAP seems to reduce blood pressure in patients with symptomatic OSA who adhere to it, its effect on blood pressure in adults with OSA who do not have daytime sleepiness is less well-established (180). The short-term effect of CPAP on blood pressure in patients with moderate to severe OSA with or without daytime sleepiness and resistant hypertension is small (3 mm Hg) and of unknown clinical benefit.

Recommendation 1: ACP recommends a sleep study for patients with unexplained daytime sleepiness. (Grade: weak recommendation, low-quality evidence)

Clinicians should target their assessment of OSA to individuals with unexplained daytime sleepiness. This assessment should include evaluation of the risk factors and common presenting symptoms for OSA. The best-documented risk factor for OSA is obesity. Clinical symptoms for OSA include unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, insomnia, and snoring. If other causes have been ruled out (for example, thyroid disease, gastroesophageal reflux disease, or other respiratory diseases), further evaluation for OSA may be warranted in patients with daytime sleepiness, which is the clinically relevant OSA symptom most responsive to treatment. Evidence is lacking on the effect of CPAP on improving other outcomes, including hypertension, diabetes, coronary heart disease events, and mortality, especially among individuals without daytime sleepiness. For guidance on treatment, clinicians should refer to the ACP guideline on management of OSA. Sleepiness questionnaires, such as the ESS, help in assessing the symptom severity of OSA but cannot assess the AHI (a necessary but not sufficient component of OSA) and lack sufficient sensitivity and specificity to replace a sleep study in diagnosing OSA.

Recommendation 2: ACP recommends polysomnography for diagnostic testing in patients suspected of obstructive sleep apnea. ACP recommends portable sleep monitors in patients without serious comorbidities as an alternative to polysomnography when polysomnography is not available for diagnostic testing. (Grade: weak recommendation, moderate-quality evidence)

Full-night, attended, in-laboratory PSG is considered the reference standard diagnostic test and is recommended in patients with suspected OSA. However, in the absence of PSG, portable monitors may be used as an alternative diagnostic test in such patients. Both the AASM and the Centers for Medicare & Medicaid Services consider an AHI score of at least 15 events per hour or at least 5 events per hour with symptoms (such as daytime somnolence and fatigue) as criteria for OSA diagnosis. Evidence shows that compared with PSG, type II, III, and IV monitors have a wide range of difference in AHI estimates. These monitors have a high positive likelihood ratio and low negative likelihood ratio for various AHI cutoff levels to predict OSA. Monitors with more channels perform better than those with fewer channels, and type IV monitors have an important limitation in that they are unable to distinguish obstructive from central sleep apnea. There is no direct evidence from head-to-head comparisons of type III and IV monitors, but indirect evidence from studies comparing each monitor with PSG suggested that type III monitors performed better than type IV monitors in predicting AHI scores suggestive of OSA. Although portable monitors

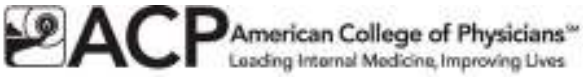
may be useful, data loss of 3% to 20% has been reported for type III and IV monitors. Furthermore, inadequate data resulting in limited interpretation of results from the use of type III monitors has been reported for 13% to 20% of the evaluations. The utility of portable monitors for patients with serious comorbid conditions, including chronic lung disease, congestive heart failure, or neurologic disorders, has not been verified.

Evidence from studies comparing one monitor with another is lacking. The Figure summarizes the recommendations and clinical considerations.

Figure.

Summary of the American College of Physicians guideline on diagnosis of OSA in adults.

AHI = apnea–hypopnea index; CHD = coronary heart disease; CPAP = continuous positive airway pressure; OSA = obstructive sleep apnea; PSG = polysomnography.



SUMMARY OF THE AMERICAN COLLEGE OF PHYSICIANS GUIDELINE ON DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA IN ADULTS

Disease/Condition	OSA
Target Audience	Internists, family physicians, and other clinicians
Target Patient Population	Adults with suspected OSA
Screening and Diagnostic Tests	PSG Type II, III, and IV portable monitors Questionnaires
Interventions	Strategies to manage OSA
Outcomes	All-cause mortality, cardiovascular mortality, nonfatal cardiovascular disease, stroke, hypertension, type 2 diabetes, postsurgical outcomes, and quality of life
Recommendations	*Recommendation 1: ACP recommends a sleep study for patients with unexplained daytime sleepiness. (weak recommendation, low-quality evidence)* *Recommendation 2: ACP recommends polysomnography for diagnostic testing in patients suspected of obstructive sleep apnea. ACP recommends portable sleep monitors in patients without serious comorbidities as an alternative to polysomnography when polysomnography is not available for diagnostic testing. (weak recommendation, moderate-quality evidence)*
High-Value Care	Clinicians should target their assessment of OSA to individuals with unexplained daytime sleepiness.
Clinical Considerations	The utility of portable monitors for diagnosing OSA in patients with comorbid conditions, such as chronic lung disease, congestive heart failure, or neurologic disorders, is unknown. Although portable monitors may be used to diagnose OSA, AHI measurements from these devices may differ significantly from those taken with PSG. CPAP treatment does not reduce CHD events and mortality in patients with OSA who do not have daytime sleepiness.

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Inconclusive Areas of Evidence

Abstract | Methods | Comparison of Diagnostic Tests for OSA | Predictors of Long-Term Clinical and Functional Outcomes | Summary | Recommendations | Inconclusive Areas of Evidence |ACP High-Value Care | References

Preoperative Screening for OSA

Detection of OSA in patients having surgery is an area of considerable interest. However, the current evidence does not provide enough information on the effect of preoperative screening for sleep apnea on surgical outcomes. Four low-quality studies provided inconclusive evidence (115, 183–185). Hence, at this point, ACP's Clinical Guidelines Committee cannot determine the benefits and harms of preoperative screening for OSA.

Phased Testing for OSA

The current evidence from 1 low-quality study was insufficient to draw conclusions about phased testing compared with full PSG testing for diagnosis of OSA.

Assessment in Patients With Comorbid Conditions

The utility of portable monitors for diagnosing OSA in patients with comorbid conditions, such as chronic lung disease, congestive heart failure, or neurologic disorders, is unknown because few studies included these patients.

ACP High-Value Care

Abstract | Methods | Comparison of Diagnostic Tests for OSA | Predictors of Long-Term Clinical and Functional Outcomes | Summary | Recommendations | Inconclusive Areas of Evidence |ACP High-Value Care | References

Evidence shows that before diagnosis, patients with OSA have higher rates of health care use, more frequent and longer hospital stays, and greater health care costs than after diagnosis (18, 186). Clinicians should target evaluation of OSA to patients with unexplained daytime sleepiness. This assessment should include evaluation of the risk factors and common presenting symptoms for OSA. The best-documented risk factor is obesity. Clinical symptoms include unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, insomnia, and snoring. Assessment of OSA in the absence of daytime sleepiness or treatment of persons with low AHI scores is low-value care because evidence to date indicates that neither improves clinical outcomes.

In the forefront

Al-Khidmat Foundation, affiliated to Jamaat-e-Islami

By Rahimullah Yusufzai

Al-Khidmat Foundation, affiliated to Jamaat-e-Islami, and Falah-e-Insaniyat Foundation, linked to Hafiz Mohammad Saeed-led Jamaatud Dawa were the first to arrive on the scene

It is a familiar story and has been repeated at every place that has suffered natural or man-made disaster in Pakistan in recent years.

Be it the earthquake of October 2005 when Hazara division in Khyber Pakhtunkhwa and Azad Kashmir were devastated, the humanitarian crisis caused by the displacement of around 2.3 million people as a result of the military operation in Swat and other districts of Malakand division in 2009, or the summer floods in most of Pakistan in 2010, the Islamic non-governmental organisations have often been the first ones to reach the site of destruction and also the most visible.

This time also, two Islamic NGOs reached Bannu ahead of others to provide assistance to the tribal people dislocated by the military operation in North Waziristan.

Al-Khidmat Foundation, affiliated to the Jamaat-e-Islami, and the Falah-e-Insaniyat Foundation (FIF), linked to Hafiz Mohammad Saeed-led Jamaatud Dawa were the first NGOs to arrive on the scene and provide a range of services to the internally displaced persons (IDPs).

Though a few others, including Pakistan Red Crescent Society, followed and started relief work, the Al-Khidmat and FIF were the most active and visible with their ambulances, medical camps and food distribution centres.

It seems the other NGOs are taking their time to organise relief and social work. Some have security concerns, others lack manpower and resources and most are more into advocacy work. Senior officials in the Khyber Pakhtunkhwa government told TNS that they have received requests from a number of social workers, philanthropists and NGOs for undertaking welfare activities for the IDPs in Bannu and other cities and towns, but were reluctant to grant permission until issues of security were addressed.

It seems the other NGOs are taking their time to organise relief and social work. Some have security concerns, others lack manpower and most are more into advocacy work.

Apparently, the Islamic NGOs have no such concerns and this is the reason their workers are the first ones to arrive at the scene after every natural or man-made disaster.

Atiqur Rahman Chohan, the FIF's coordinator for relief work in Khyber Pakhtunkhwa, told TNS that they were on the spot in Bannu on June 16 a day after the military operation was launched in neighbouring North Waziristan. "We have a network of FIF in almost every district of Pakistan. We already had a strong presence in Bannu, Dera Ismail Khan, Tank and Lakki Marwat districts and I was able to mobilise my staff and volunteers in no time. We have stocks of food and non-food supplies and it didn't take us long to transport the needed items to Bannu," he explained.

The figures provided by Chohan about the FIF's relief work were impressive. He said 145,000 displaced persons had been provided cooked food to-date, 15,000 received medical care, four static and two medical units are operational with trained doctors, paramedics and operation theatres, and eight ambulances are available round-the-clock for patients. He said 10,000 IDPs were provided

food at Sehar and Iftar and 125 maunds of dates and packets of dry food items have been distributed.

The FIF also managed to open a distribution centre in Dera Ismail Khan and is ready to expand its relief work on need basis. “We started giving tarpaulins to the IDPs when they refused to stay in the small suffocating tents set up by the government in Bakkakhel so that they could use it for shade and also get some ventilation,” Chohan added.

When asked whether they were stopped by the government or security forces from doing relief work, the FIF official said nobody created hindrance in their activities. “The people in Dera Ismail Khan staged a rally in our support when the US recently imposed sanctions on Jamaat-ud-Dawa and some of its members. Our work is appreciated and it is due to the trust in FIF that traders and common people give us donations in cash and kind,” he argued.

As for Al-Khidmat Foundation, it isn’t controversial as its patron, Jamaat-e-Islami, is working legally and peacefully. The FIF’s links with Jamaat-ud-Dawa, which in turn has been linked to Lashkar-i-Taiba, makes its work controversial. The Al-Khidmat Foundation, headed by Dr Hafeez-ur-Rahman, claims to be the biggest welfare and charity organization in Pakistan as it is running schools, hospitals and many other projects. Its work has been recognized internationally and the government of Japan too gave it a generous donation for relief work during the 2010 floods.

Other political parties, too, have established their social welfare and charity organizations, but the MQM’s Khidmat-e-Khalq Foundation, ANP’s Bacha Khan Trust and the PPP’s Shaheed Bhutto Foundation have yet to mobilise volunteers and do relief work in support of the North Waziristan IDPs. They have left the field wide open for the Islamic NGOs, which have thrived in recent years and expanded their network having hundreds of volunteers and huge amounts of funds.

Doctors tackle damaged minds in Gaza

In a ward at Shifa, Gaza's largest hospital, child therapist Rabeea Hamouda is trying to elicit a response from two small brothers, Omar and Mohammed, aged three and 18 months, hoping for some words or perhaps a smile.

For seven straight minutes the children, peppered with burns and shrapnel wounds sustained in Israeli shelling that hit their home in north Gaza, stare at him blankly, emotionless.

Eventually, as Hamouda gently teases them, pretending to mix up their names and holding out a present while another counsellor sings quietly, a smile creeps across Mohammed's face and the older one, Omar, cries out his name.

"At the beginning, Omar was not responding to us at all, he was not even willing to say his name," explains Hamouda, who heads a team of 150 psychotherapists working for the Palestinian Centre for Democracy and Conflict Resolution in Gaza.

"Big progress has been made with these children," he says with a sense of relief and quiet accomplishment. "At the beginning they did not talk, they refused to communicate. But now, with the sixth session, we are witnessing good progress.

"Omar and Mohammed are just two of the 400,000 Gazan children the United Nations estimates are in need of psychological care as a result of not just the latest war in the territory but the three previous conflicts fought with Israel since 2006.The most recent conflagration has been the deadliest, with 1,945 Palestinians killed, many of them civilians and including an estimated 457 children. On the other side of the border, some 64 Israeli soldiers and three civilians have been killed.

Whether the result of Israeli air strikes, having parents or relatives killed before their eyes, hearing militants firing rockets from their own towns or themselves being wounded, the psychological trauma for Gaza's young is profound.

The symptoms range from nightmares, bed-wetting and behavioural regression to more debilitating mental anxiety, including an inability to process or verbalise experiences.

There is also deep trauma on the other side of the border, with tens of thousands of Israeli children mentally disturbed by the regular rocket fire from militants during the month-long war and over the seven years since Hamas seized control of Gaza.

While the conflict's destruction of buildings and livelihoods is clear to see and documented daily in television footage, the damage to minds is mostly invisible, yet can have far more damaging and longer-lasting consequences.

"The first time a child goes through a traumatic event like a war it's just deeply terrifying," said Chris Gunness, the spokesman of the United Nations Relief and Works Agency, which has 200 psychotherapists working in up to 90 clinics in Gaza.

"The second time is terrifying-plus-one because the child remembers the worst parts of the last war as well as the impact of the current one. Then the third time is plus-plus as the compounded memories of conflict build up.

"This time, for an eight- or nine-year-old child in Gaza, it's very, very intense indeed because there is this cumulative toll of trauma from repeated conflicts since 2006."

Hamouda and his team, like other psychotherapy units working across the small territory - home to an estimated 1.8 million people, more than half of whom are aged under 18 - can barely cope with the number of patients requiring help.

The treatment is by necessity basic - an effort to draw children out, to have them paint pictures of their experiences or emotions, to get them to verbalise their circumstances.

While a lot can be achieved with such simple techniques, many more require longer-term, personalised psychological care because of the enormity of the mental damage suffered.

"First we provide wounded and traumatised children with immediate pyscho-social support and we give parents some guidance on how to deal with them," says Hamouda. Then there is home care and follow up for the more severe cases.

"Houses can be rebuilt and some physical wounds can be healed, but the people's psychological condition needs more than money and time," he says. "It needs a big effort and persuasion, and overall it needs calm and stability."

One of Gaza's most successful trauma assistance projects is the Gaza Community Mental Health Programme, launched in 1990.

Hassan Zyada, a psychologist with the project, describes the latest conflict as easily the worst since 2006, with scores of Palestinians having lost multiple family members.

"Our expectation is that more than 30 percent of the people here in Gaza will develop a psychiatric disorder," he said.

Even health professionals are not immune. Six members of Zyada's own family were killed during the war: his mother, three brothers, a sister-in-law and a nephew. He is now receiving counselling from the clinic's chief therapist.

"It is a really traumatic loss and it is not easy for me to deal with," he said, adding that several others on the team had suffered similar experiences.

FDA panel backs limiting use of testosterone replacement drugs

By Toni Clarke

(Reuters) - Testosterone replacement therapies should be reserved for men with specific medical conditions that impair function of the testicles, an advisory panel to the U.S. Food and Drug Administration concluded on Wednesday.

The FDA is not obliged to follow the advice of its advisory panels but typically does so. The panel also recommended that companies be required to conduct additional studies to assess the cardiovascular risk of their products for patients with age-related low testosterone.

Prescriptions for "Low T," as low testosterone has been described in television commercials, have soared over the past decade, driven by an increase in use by middle-aged men with lowered testosterone levels related to advancing age.

Symptoms of low testosterone include loss of libido, decreased muscle mass, fatigue and depression.

The panel voted 20-1 in favor of restricting the drugs' authorization to people with medically related low testosterone, such as a genetic disorder or a tumor.

If implemented, the restriction would mean companies could not market or promote their products for age-related low testosterone, although physicians would allowed to prescribe products "off label" in any way they choose.

Fourteen members of the panel voted in favor of additional safety studies to assess potential cardiovascular risks associated with the drugs in patients with age-related low testosterone.

Four panelists recommended that cardiovascular studies be conducted regardless of the population in which they are used. One member voted against the need for a study. Most panelists said any safety study should be large and randomly controlled, the gold standard for assessing safety and efficacy.

The market for testosterone treatments currently includes skin patches, short-acting injections and topical gels. AbbVie Inc's AndroGel, the market leader, generated about $1.04 billion in sales in 2013. Other products include Auxilium Pharmaceuticals Inc's Testim and Eli Lilly & Co's Axiron.

On Thursday, an FDA advisory panel will consider Rextoro, a product being developed by privately held Clarus Therapeutics Inc. which, if approved, would be the first oral treatment to meaningfully challenge existing treatments.

In a preliminary review of the data published on Tuesday, FDA reviewers said that although the Rextoro drug met the main goal of a clinical trial, a separate analysis by the FDA that accounted for missing data found it was not as effective as it might appear.

RISE IN PRESCRIPTIONS

In 2013, 2.3 million men received a prescription for testosterone, up from 1.3 million in 2010, according to the FDA. About 70 percent of men prescribed testosterone drugs were between the ages of 40 and 64.

According to an FDA analysis, 21 percent of patients prescribed testosterone drugs did not appear to have had their testosterone concentrations tested before or during treatment, something the agency described as "concerning."

In February, the consumer watchdog Public Citizen petitioned the FDA to immediately add a black box warning, the most serious available, about heart risks associated with the drugs.

The FDA denied the petition, saying it was still assessing the potential cardiovascular risks of the products. Most panelists said a black box warning would not be appropriate at this time because there was not enough data to assess the level of risk.

Some recommended adding more moderate language to the label noting that the FDA is exploring whether there is a heart risk but that the evidence to date is inconclusive.

Officials for AbbVie argued that there was no evidence of a causal relationship between testosterone replacement therapies and cardiovascular problems, but said more information would be useful and that companies would be willing to discuss changes to the drug labels.

(Reporting by Toni Clarke in Washington; Editing by Jim Loney and Peter Cooney)

Migraine Rx in the ED: A Systematic Review

September 02, 2014 | Headache and Migraine

By Thomas P. Bravo, MD and David W. Dodick, MD

Migraine headache accounts for at least one-third of the 5,000,000 headache visits to US emergency departments each year. In the acute care setting there is currently significant heterogeneity in the treatment of acute migraine. This practice variation can result in patients being treated with medications that may be ineffective and can contribute to prolonged ED stay, poor patient outcomes, return visits to the ED, and worsening of the migraine pattern.

Recently a systematic review examined the available literature on acute care treatments for migraine for effectiveness and tolerability, graded each medication's level of available evidence, and gave recommendations regarding its use.[1] The review was limited to double-blind prospective RCTs in adults treated in an emergency department or equivalent acute care setting. Only studies that defined migraine using either International Headache Society diagnostic criteria or the Ad Hoc criteria were included. Overall 831 abstracts were screened, 120 full text articles were assessed resulting in a total of 44 studies included in the review. Each study was graded according to risk for bias and given a final rating of methodological quality using the US Preventative Task Force criteria.

Recommendations regarding use of each treatment were made at a consensus meeting of the Canadian Headache Society. This expert consensus group reviewed each treatment based on several additional factors including desirable and undesirable side effects, variability in patient values or preferences, and wise use of resources. The level of quality of evidence had partial impact on the use recommendation. Final use recommendation was graded as strong or weak based on review of these additional factors. The pertinent results are summarized in the **Table**.

Five therapies (4 available in the US) with high to low levels of evidence gained a strong recommendation for use.

Prochlorperazine (Compazine) carried the highest level of evidence based on 2 "good," 3 "fair," and 1"poor" trials. The authors note that although strongly effective, this should be weighed against the relative frequent occurrence of extrapyramidal symptoms (EPS). In one study, EPS occurred in both prochlorperazine and metoclopramide groups in 13% of treated subjects. To address this, consideration of coadministration with an agent such as diphenhydramine is advised.

Subcutaneous sumatriptan was the only triptan medication assessed in this review. While carrying a strong recommendation, it is more likely to be efficacious when given in the first few hours after the onset of a migraine attack and is limited to patients who have not used a triptan in the last 24 hours. Despite their effectiveness, triptans are currently underutilized; a recent analysis of a National Hospital Ambulatory Medical survey found a triptan medication was given only in 7% of

acute migraine treatments in the ED. Additionally when a triptan was used, the median length of ED stay was shorter than when opiate therapy was administered.[2]
Ketorolac (IM or IV) was strongly recommended after 2 "fair" and 2 "poor" quality studies with active comparators.

One of the more striking results of the review is the recognition that the evidence on comparative efficacy of available options is generally of low quality. Many treatments received weak recommendations based on the very limited evidence available.

Meperidine (Demerol) received a weak recommendation based on 1 "fair" and 1 "poor" study. Despite falling softly into the "use" category, meperidine is becoming much less available due to concerns of serious adverse events, including seizure. It is recommended that this drug be used with caution.

Routine use of opioids has long been advised against for acute migraine.[3]
The limitation in scope of this review was again demonstrated in the evaluation of dexamethasone. This medication received a strong recommendation with moderate evidence that it is *not* effective in acute treatment. However some evidence suggests that a single dose acutely will decrease the relative risk of migraine recurrence 26% over the first 72 hours, overall making it potentially beneficial outside of its immediate effect.[4]
Overall this systematic review is a substantial step forward in establishing an evidence-based approach to migraine treatment in the acute care setting. It demonstrates that there is significant need for further research. While clinicians should exercise judgment based on each individual patient and circumstance, this review provides an excellent evidence based guide.

Table.

Treatment	Discussed Dose	Recommendation Strength	Level of Evidence
Recommended for use in acute migraine relief in ED or similar settings (use)			
Prochlorperazine	10 mg IV	Strong	High
Metoclopramide	10 to 20 mg IV	Strong	Moderate
Sumatriptan	6 mg SC	Strong	Moderate
Ketorolac	30 mg IV to 60 mg IM	Strong	Low
Chlorpromazine	0.1 mg/kg to 25 mg IV	Weak	Moderate

Dihydroergotamine	1 mg SC or IM	Weak	Low
Lidocaine intranasal	40 to 80 mg	Weak	Low
Meperidine[a]	75 to 100 mg IM	Weak	Low
Not recommended for use in acute migraine relief in ED or similar settings (do not use)			
Dexamethasone IV[b]	-	Strong	Moderate
Granisetron IV	-	Strong	Low
Haloperidol IV	-	Strong	Low
Acetaminophen IV	-	Weak	Moderate
Magnesium sulfate IV	-	Weak	Moderate
Octreotide IV	-	Weak	Moderate
Diclofenac IM	-	Weak	Low
Droperidol IM	-	Weak	Low
Lidocaine IV	-	Weak	Low
Morphine IV	-	Weak	Low
Propofol IV	-	Weak	Low
Sodium valproate IV	-	Weak	Low

[a]Caution given potential serious side effects; [b]may be helpful for migraine recurrence

Adapted from Table 3, Orr et al.[1]

Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence.

Abstract

OBJECTIVE:

To examine the effectiveness of parenteral corticosteroids for the relief of acute severe migraine headache and prevention of recurrent headaches.

DESIGN:

Meta-analysis.

DATA SOURCES:

Electronic databases (Cochrane Central Register of Controlled Trials, Medline, Embase, LILACS, and CINAHL), conference proceedings, clinical practice guidelines, contacts with industry, and correspondence with authors.

SELECTION CRITERIA:

Randomised controlled trials in which corticosteroids (alone or combined with standard abortive therapy) were compared with placebo or any other standard treatment for acute migraine in adults.

REVIEW METHODS:

Two reviewers independently assessed relevance, inclusion, and study quality. Weighted mean differences and relative risks were calculated and are reported with 95% confidence intervals.

RESULTS:

From 666 potentially relevant abstracts, seven studies met the inclusion criteria. All included trials used standard abortive therapy and subsequently compared single dose parenteral dexamethasone with placebo, examining pain relief and recurrence of headache within 72 hours. Dexamethasone and placebo provided similar acute pain reduction (weighted mean difference 0.37, 95% confidence interval -0.20 to 0.94). Dexamethasone was, however, more effective than placebo in reducing recurrence rates (relative risk 0.74, 95% confidence interval 0.60 to 0.90). Side effect profiles between dexamethasone and placebo groups were similar.

CONCLUSION:

When added to standard abortive therapy for migraine headache, single dose parenteral dexamethasone is associated with a 26% relative reduction in headache recurrence (number needed to treat=9) within 72 hours.

The Monoaminergic System and Its Putative Role in Alzheimer Disease

By Derick E. Vergne, MD

β-Amyloid plaques are believed to accumulate in the early stages of Alzheimer disease, leading to the development of symptoms, such as memory loss. The plaques occur when enzymatic proteolysis of the amyloid precursor protein (APP) by β-secretase forms the toxic misfolded oligomer β-amyloid.

To build on previous findings on the effects of citalopram on β-amyloid plaques, Sheline and colleagues[1] evaluated the role of the serotonergic system in an animal model of Alzheimer pathology as well in healthy human volunteers. Citalopram was found to halt the growth of existing β-amyloid plaques and reduce the formation of new ones by 78%; the drug also decreased β-amyloid in the cerebrospinal fluid in healthy adults.

Although these findings are important and point to a different direction for research, what makes it perhaps all the more interesting is the drug used. Citalopram is an SSRI and its mode of action, although not entirely clear, begins with blockade of the serotonin transporter—a protein that transfers serotonin from the synaptic cleft to the presynaptic neuron. Its therapeutic mode of action is therefore, at least initially, to modulate the serotonergic system by way of its receptors.

Relatively recent research has pointed to downstream effects in cellular architecture as well as at gene level.[2] More striking is the finding that SSRIs relieve depression by inducing the proliferation of brain-derived neurotropic factor. Ultimately, the relief of depression has been associated with the degree of neurogenesis—a revolutionary finding given that the brain has been understood to be static in adults. If citalopram is theoretically capable of relieving depression by promoting neurogenesis, could that be an explanation for the findings in the study by Sheline and colleagues? It is clearly not that easy; neurogenesis and the associated relief of depression occurs over 6 to 8 weeks, and the researchers saw a decrease in β-amyloid formation even after 1 dose of citalopram. Therefore, antidepressant efficacy does not necessarily equate to potential Alzheimer prophylaxis.

The monoamine system in the prevention of plaque formation

Other SSRIs might have the same effect on plaque formation as citalopram.[3] Looking at the way SSRIs affect the serotonergic system may help us understand how SSRIs affect plaque formation—which receptors and second messenger molecules are involved. Pimenova and colleagues[4] found that agonists that activate the serotonin 4 receptor induce the up-regulation of α-secretase activity. This action leads to the cleavage of APP into a soluble (good) fragment by way of downstream activation of other intracellular messenger systems.[3,4] α-Secretase is a proteolytic enzyme that

unlike β-secretase cleaves APP into a soluble and neuroprotective APP fragment form (sαAPP), therefore precluding the formation of the amyloidogenic counterpart β-amyloid peptide.[5]

The implication of the study by Pimenova and colleagues[4] is that serotonin 4 activation would be an initial step in the appropriate cleavage of APP by α-secretase. Despite the link between serotonin, the serotonin 4 receptor, and α-secretase, citalopram is not known to be an agonist or antagonist at the serotonin 4 receptor. One way of reconciling these facts is to think that the initial effect of the SSRIs (not the effects that tend to work for depression, at least initially) is to acutely increase the density of intrasynaptic serotonin. The resulting increase in serotonin density increases the probability of it stimulating other serotonin receptors; therefore, a putative agonism on serotonin 4 would be indirect.

It appears that the extracellular regulated kinase cascade is a key player in the link between serotonin and α-secretase, since its inhibition by experimental manipulation is capable of reversing serotonin-induced β-amyloid reduction.[3] The serotonin 4 receptor is another player; it is likely that other serotonergic receptors will end up being as important.

The muscarinic cholinergic system

The cholinergic system plays a key role in learning, memory, and overall cognition. Attempts at enhancing cholinergic neurotransmission are at the heart of common first-line treatments for Alzheimer disease. What is now becoming clear is that the muscarinic cholinergic receptor M1 appears to play a prominent role in augmenting the activity of α-secretase to form the sαAPP oligomer. Pharmacological and behavioral paradigms using agonists and antagonists for the M1 receptor have improved and worsened, respectively, cognitive parameters in animal models, and in vitro analyses have revealed the role of M1 on α-secretase activity.[6]

Citalopram has been shown to partially target the cholinergic system.[7] For instance, citalopram is known to reverse memory impairment by way of increasing acetylcholine activity in the hippocampus in animal models. It has been hypothesized that citalopram improves memory in depressed patients, at least in part, by its modulation of the cholinergic system. The **Table** presents a summary of key findings from citalopram research in Alzheimer disease.

Conclusion

The SSRIs, although principally targeting serotonin transporter, are complex drugs that might work on other neurotransmitter and receptor systems. It is likely worthwhile to look at the effects of other monoamine and neuropeptide systems on the enzymatic machinery cleaving APP. Further studies are needed to clarify the effects that other well-know compounds currently used in neuropsychiatry could have in alleviating Alzheimer disease.

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