Jonathan Cole's letter to Jay Amsterdam on Insulin Coma Treatment
Collated by Olaf Fjetland

This collated document includes Jonathan Cole's March 16, 2004 letter to Jay Amsterdam on Insulin Coma Treatment posted on February 21, 2019 and the exchange that followed the posting of this document.

Six INHN members participated in the exchange: Jay Amsterdam, Tom Ban, Max Fink, Samuel Gershon, Janusz Rybakowski and Shridhar Sharma exchanged a total of seven postings. The last entry in this exchange was made on September 17, 2020.

This collated document is now open for a final comment to all INHN members.

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Jonathan Cole's letter to Jay Amsterdam on Insulin Coma Treatment

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March 16, 2004

Jay Amsterdam, M.D.
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Dear Jay,

Reading your excellent chapter in the course of reviewing the Wolkowitz-Rothschild book on Psychoeuroendocrinology reminded me that you (or your co-author) might be our excellent service of advise regarding my current expanding project to try to clarify and document insulin coma therapy. I ran an IC Unit at Ft. Bragg Army Hospital in 1952-53 and pre-drugs, felt ICT was much better than standard care (in 1948-51) at Payne Whitney or ECT at Ft. Bragg.

1) Do you have Russian Psychiatric contacts? I understand that insulin coma never stopped in Russia and has been used side by side with neuroleptics and ECT for decades. Do you know anyone appropriate to ask about this issue? I have no Russian but I have access to a translator and some ex-Russian friends who are now psychiatrists.

2) Do you have any idea how insulin coma might work? I'm enclosing a copy of the VA Technical Bulletin I used to give ICT way back and a copy of the Fink paper on John Nash's prolonged but temporary recovery after ICT. I think the controlled comparative studies of ECT are flawed and if redone properly might come out differently. I hear Dr. Belmaker in Israel had been trying to originate such a trial.

I'm delighted that the Eldepryl patch seems likely to be prescribable soon.

With best regards,

Jonathan O Cole MD

Jonathan O. Cole, M.D.

February 21, 2019

Jay Amsterdam's email to Tom Ban with copy to Max Fink (October 29-30, 2018)

I recently came across another, potentially historical, gem that follows on to the recent INHN running commentary about insulin coma therapy. I thought that this letter from Jonathan Cole may be of some interest to you, as well as to Max Fink (who makes a cameo appearance in it). In the letter, Dr. Cole refers to a chapter that my (then) post-doctoral fellow and I wrote for Owen Wolkowitz's book on psychoneuroendocrinology (published by the American Psychiatric Press in 2002). I have located the galley proof of the chapter and have also attached it.

When I have a few free moments, I will try to search through old computer files from the time of the letter (i.e., 2004) to see if I can locate any response from me to Dr. Cole.

I hope you enjoy this little slice of neuropsychopharmacology history.

March 7, 2019

Max Fink's comment on Jay Amsterdam's e-mail to Tom Ban (October 29-30, 2018)

Thank you for the reminiscence of Jonathan Cole's broad view of psychopharmacology that, for him, included insulin coma therapy. He had personal experience with the procedure and was puzzled by the potential mechanisms. The theories included Manfred Sakel's Nazi concept that insulin selectively killed off the "bad" neurons of psychosis, the effects on memory (similar to ECT) and my thoughts that the limited efficacy was based on the induced seizures, that ICT was a weak form of Metrazole or ECT seizures. He urged me and others (Haim Belmaker) to develop clinical studies. By that time, I had published my RCT of ICT and CPZ, concluding that ICT was a high risk, occasionally fatal, riskful treatment that was no longer justified.

At a later date I was consulted on the insulin coma applied to the Nobelist John Nash as described in the biography and film A Beautiful Mind. The filmmakers showed the induced seizure in the film. Alas, the benefits of the treatment were transient. Attempts to sustain the benefits with CPZ devastated Nash physically and mentally. As Sylvia Nasar wrote in the biography, Nash was offered ECT. His Princeton colleagues dreaded the damage to "this beautiful mind" and convinced his wife to refuse consent. (After reading the history and seeing a Nash interview, ECT as we were then learning to do, with C-ECT as an part of the treatment course, would have benefitted him much, since he met the criteria for catatonia, a treatable syndrome.)

Jonathan Cole also was a supporter of the science of pharmaco-EEG, funding worldwide studies that identified many active entities (mianserin, 6-aza-mianserin). discarded as inactive

(flutroline), reclassified more appropriately for marketing (doxepin). When presented with a request for funding of a unproven methodology that required an IBM 1800 computer system (about $1,000,000) he did not flinch but organized funding across the NIH Institutes. He had also funded (by a $10,000 supplement) an electronic frequency analyzer at Hillside Hospital in 1958 through the ECDEU system.

March 7, 2019

Shridhar Sharma's comment on Fink's comments

Thank you for asking me to comment on Max Fink's comment on Jonathan Cole's letter regarding Insulin Coma Treatment (ICT).

I did not know Max Fink personally but on few occasions met him during American Psychiatric Association and World Psychiatric Association meetings. His views on the use of electro convulsive therapy (ECT) were more prominent and he was a supporter of ECT. His views on ICT, however, were mixed. He believed ICT acted similarly to Metrazol, but he believed ICT was a high-risk treatment, occasionally fatal. He had personal experience using ICT especially in catatonic schizophrenia but, like other researchers, was not clear about the potential mechanism of action. Dr. Fink earlier believed the ICT seizures improve the outlook in schizophrenic patients, similar to ECT.

Seizure did occur during ICT, appearing in the second and third stage of coma, especially during periods of Dry Coma. Two schools of thought developed: 1) those who thought that seizure, like in ECT, was favorable for a better outcome; and 2) those who considered seizure as an unwanted side effect.

I agree with Max Fink's view that although ICT was high risk and occasionally fatal in the mid-20th Century it was safe in hands of experts and effective when applied in good monitoring facilities.

August 1, 2019

Jay Amsterdam's e-mail to Janusz Rybakowski on March 2, 2019

Dear Janusz,

I may have written to you about this issue back in the early 2000s when I received a letter from Jonathan Cole. I did not know of anyone in Russia who was treating depressed patients with insulin coma therapy (ICT). However, I did know of you and I would have written to you to see if you could be helpful to me in providing Jonathan with the answer to his query about current (in the 1990s and 2000s) use of ICT in Eastern Europe.

Alas, I no longer have any of Jonathan's other items that he mentions that he sent to me; and the letters that I have from you do not mention anything about ICT.

It also appears from Jonathan's letter that he was wondering if I thought that there might be some endocrine marker (beside the DST) that might show how ICT may facilitate antidepressant effect. I recently re-read the chapter that Mady and I wrote to see if I could find a neuroendocrine connection with ICT; however, I could not find anything that I thought may be a neuroendocrine probe.

Tom Ban (and perhaps Max Fink) is quite keen to revisit this issue for posting on the INHN web-site. Thus, I have also attached the chapter that Jonathan and Tom make reference to from Owen Wolkowitz' book.

Do you have any thoughts on the issue of neuroendocrine markers and ICT from the attached (or other) sources? If so, I would be very interested in knowing them; and perhaps writing a reply to Max Fink's recent commentary on the Jonathan Cole letter that was posted several weeks ago on INHN.

As ever, I send you my warmest, personal greetings and affection,

Jay

June 11, 2019

Janusz Rybakowski's reply to Jay Amsterdam on March 3, 2019

Dear Jay,

Thank you for your letter. Unfortunately, I do not have any knowledge on the ICT except for reminding that this therapy was used in Poland (Lublin) in 1960.

Presently, I am waiting for announcing the date of the ISBD meeting in 2020 which is going to be held in Chicago.

God willing, I would plan to go to this conference, and, after this, to drop for several days to Philly, to visit my old friends.

Best greetings: Janusz

June 11, 2019

Tom Ban's e-mail to Max Fink On June 11, 2019

Dear Max,

You might have noted already that Jay Amsterdam's e-mail exchange with Janusz Rybakowsky relevant to Jon Cole's e-mail to him several years ago with his e-mail to us relevant to same was posted this week. Please find in the attachment an updated collating document of this project.

Warm regards,

Tom

December 5, 2019

Max Fink's reply to Tom Ban on June 12, 2009

Dear Tom,

The interest and use of insulin coma therapy that began in 1933 ended with the introduction of chlorpromazine. The Hillside Hospital RCT of ICT and CPZ offered well studied evidence that CPZ was as effective, with fewer adverse events, and much less expensive than ICT. The JAMA 1958 report is attached.

By the mid-1960s the era had ended, although reports of continued use in China and Russia occasionally surfaced. I recall a transient blip in interest in Israel with the flood of Russian Jewish emigres in the 1990s by Haim Belmaker, but the excitement was unproductive.

The single best explanation of ICT efficacy was its singular induction of grand mal seizures, reported between 5% and 20% of coma inductions. In my ICT days, senior MDs who admitted

patients often added ECT seizures to comas for the very psychotic ill. ICT as a weaker form of ECT, much like the much-touted MST — magnetic seizure therapy — that has a small cadre of supporters at NIMH (Susan Lisanby) and Germany (Thomas Schlaepfer).

Best regards

Max

December 5, 2019

Samuel Gershon's e-mail to Jay Amsterdam and Tom Ban with copy to Max Fink on July 11, 2019

This topic and its discussion are important to illustrate the need for psychiatry to demand a more critical assessment of findings that too quickly become accepted as the best treatment available for whatever. I went to Dr, Cade's hospital in Melbourne because of his paper on lithium treatment. I was informed that by that time he had banned its use because of toxicity, that's another story.

But back to this topic. A fellow resident and I were assigned to work in in the ICT unit and then follow the patients in the Outpatient Department. We both felt that after ICT the patients were in much better physical condition, but over the time we followed them as outpatients they returned to their pre-treatment symptoms. We both went to speak to our teachers and were told quite firmly that ICT was the specific treatment for schizophrenia and what did we know — a cautionary warning. Over the next few years I had the opportunity to travel and found (as stated in the correspondence above) that in every country I went, ICT was the specific treatment for this condition

It was clear this was a pandemic delusion.

Then in 1959, a group at the Maudsley compared ICT versus barbiturate sleep and found no significant difference.

So, psychiatry needs to be aware of the next wonder treatment.

Regards, Sam

December 5, 2019

Jay Amsterdam's e-mail to Max Fink on July 11, 2019

Dear Max:

Thank you so much for sending along your thoughtful comments on ICT.

I just re-read, with renewed interest, your seminal article comparing ICT to CPZ from JAMA 1958. In many respects, this article itself is an important, if unrecognized, slice of psychiatric research history for our field. In this regard, it harks back to a time when psychiatry researchers published the unvarnished truth of their experimental observations (and did not simply provide some post hoc, "positive," whitewashed and doctored outcome of the study results in order to facilitate its publication in a high-impact journal).

In fact, as I now re-read through your JAMA article, I wondered whether the observations that you reported would even be considered by most of today's journal editors for the peer-review process, much less for publication. In this regard, I wonder if JAMA, or any of our other current tier 1-4 psychiatry research journals, would even consider publishing your "negative" findings (which proved so consequential for the field of psychiatry). It would surely be a tough uphill battle for you to get such a manuscript published. And just imagine the uphill publication struggle that would be experienced if you had performed this same experiment today and had chosen an atypical antipsychotic for a comparator to ICT! I fear that the unrecognized publication pressures that are now brought to bear upon investigators by academic institutions and their publication imperatives, the largess of Pharma grants to these investigators and their institutions, the pressures to solidify potential business partnerships between academic and industry stake holders and the financial support of Pharma industry to the editors and owners of scientific journals would surely mitigate against the likelihood of you getting your excellent experimental observations published. Moreover, "negative" findings are akin to "bad news" which does not sell journals or journal subscriptions; does not facilitate the placement of Pharma advertisements in journals or other financial support for future journal publications; and does not result in high journal impact factors, which result in high journal income.

Furthermore, your post hoc finding, from a decade earlier, that "usual care" for these psychosis patients results in a similar outcome to the two unique interventions would also not bode well for the likelihood of you getting your excellent research findings published. And finally, of course, there's the looming (but at the time, in 1958, completely unknown) issue of the tardive adverse effects of neuroleptic drugs, like CPZ (and all of its successors).

Although I may sound a bit cynical, I have always wondered over the past 45 years of my reading various psychiatry reports (like that of your excellent article), how few "negative" findings were ever published in psychiatric research journals and how vast was the surfeit of interesting "positive" findings that were published – although it was always a conundrum to me just how little clinical progress all of these positive findings made to our field writ large.

In any event, as one of the last living clinical purveyors and researchers of ICT in our field, I thank you for your continued wisdom and insight on this topic.

With my very best wishes,

Jay

December 5, 2019

Max Fink's comment on Sam Gershon's e-mail to Jay Amsterdam with copies to Jay Amsterdam and Tom Ban

Insulin Coma Therapy (ICT) was a high nursing care treatment. In retrospect, it acted as a weak form of electroshock. Many patients, especially the more severely ill , were much improved but we did not have a maintenance treatment (that we now have in continuation OPD ECT).

ICT was the best available Rx for psychosis until CPZ appeared. No, not a pandemic delusion, but the best available, weak toxic treatment.

Regards, Max

December 5, 2019

Samuel Gershon's final comment

I have nothing to add to this thread but to restate my experiences around the world. I saw it as the "standard" and "established " treatment for schizophrenia in Australia, say from 1948, and in Melbourne in the early 1950s and through the 60s. I saw it as the established treatment in England, Russia and Israel.

In Melbourne, as residents, we followed patients through its admission, ICT and follow- ups; during this last phase they really began to unwrap.

As I have said before, it was universally accepted as the one specific treatment for schizophrenia and at that time my colleagues and I thought it was a Pandemic Delusion and a serious black mark against the profession. One must also remember, it carried a risk of serious side effects, including death.

September 17, 2020