THE FOUNDATION OF THE BRITISH ASSOCIATION FOR PSYCHOPHARMACOLOGY
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Reading the Clinical Journal in 1974, it seems as though some of the first meetings of the BAP were recorded. Have those recordings survived?
Not that I know of. Some acquaintance of one of us asked if he could record it but when he found we didn't have any money to pay him - that was the last we ever heard of him.

Pity about that. It would have been nice to have some record. What do you remember of the foundation of the BAP
To begin with George Beaumont's description as far as it goes is pretty accurate. From my point of view I first conceived an idea of forming a British Association of some kind or other because at that time I had a grant from the US National Institute for Mental Health (NIMH). I had that for 12 years to do psychotropic drug trials in general practice because they couldn't do it in the USA. It was written into the grant that I should attend 2 meetings a year, one of which was the American College of Neuropsychopharmacology (ACNP) which was held usually in Puerto Rico in December.

Now as a result of going to those meetings I learnt quite a bit about the ACNP and how it was set up. At that time, they hadn't been going for very long, I think only about 4 years, and they were rather concerned because they had one pharmaceutical company sponsorship, I think it was Geigy, and they were really dependant on the one company for money. So they decided it wouldn't do and they established a corporate membership, which meant that any pharmaceutical company could pay, I think it was $1000, and that entitled one of their staff to attend the ACNP meetings. There had been a lot of dissension over this - a lot of people felt they were too dependent on the pharmaceutical industry so when we were discussing setting up the BAP we had this very much in mind. This is quite important as you will see given what ultimately happened.

Well I first was thinking about this at the CINP meeting in Prague and I mentioned it to Alec Coppen. This as far as I was concerned was the first, if you like, discussion of the idea with anybody else and he agreed it was a jolly good idea and lets go ahead with it. Well as so often happens nothing was done until the next CINP meeting which was held in Copenhagen. Now in the mean time I had become very friendly with Anthony Horden, who was then a consultant psychiatrist at Kings, and he came to that meeting. He hadn't been to one before. I took him as my guest and he was rather horrified to find that the bulk of the meeting was concerned with basic research and that there was very little clinical material. So that also we had in mind when we came to discuss the BAP again. After that meeting I got together with Anthony Horden - we were really the originators of it - and we discussed it and I thought well we must go ahead and do something about it.

So we had these two important facts in mind. Firstly we would be rather wary of what arrangement we might have with the pharmaceutical industry and secondly we wanted it to be a clinical association and those two facts led to a lot of the problems we had. Anyway, to cut it short, I in fact composed the letter outlining the intention to form a British Academy of Psychopharmacology. I approached various other people and of course they were notable as being clinicians but with one obvious exception and that was Malcolm Lader. How we missed him I don't know. Well this of course upset the basic scientists, particularly Philip Bradley who was a very good friend of mine actually. I remember at one meeting, I think it was at the Paris

CINP, he came over shaking his head and looking dolefully at me saying "David what have you done, what have you done". He said "I wouldn't have minded if you called it (it was called the Academy in those days) the Academy of Clinical Psychopharmacology". Of course he had a good point there. Anyway he got together with Malcolm Lader and with various other basic science people and they were threatening to set up a rival organisation. Well, as it happened a long acrimonious correspondence went on between Max Hamilton and Philip Bradley. At one time they were hardly speaking to one another. However it all got smoothed out and we realised this error and so of course we opened the doors to the basic scientists and also to anyone who had an interest in psychopharmacology.

Can I go back and ask you more about the other people whose names are on the letter and how they came to be there -Sidney Brandon from an alphabetical point of view was the first. Did you have reasons for this particular group
Yes it was alphabetical. Anthony Hordern and myself drew up the list. We thought they were people who would be interested in the idea of setting it up. They were people we knew personally, who were perhaps fairly eminent in the field of psychopharmacology and doing research in psychopharmacology.

As regards eminence in the field, one of the curious things about the foundation of the BAP and a flavour that comes through when one talks to the people involved in the start, is that well yes you picked the people like Alec Coppen who were doing the work and who were well known but on the other hand they weren't at Oxford, Cambridge or the Maudsley - they weren't part of the established centres as it were. This seems somewhat strange. Any ideas?
There was no particular reason it was just people we knew who we thought would be keen on the idea and would co-operate and in fact that's what happened.

Do you think there's anything about psychopharmacology that means that it is something that can often happen better outside the established centres of excellence.
No we didn't have any ideas like that at all. The people we chose were just people we thought would support the establishment of a psychopharmacology organisation. We didn't want the organisation to be a Society because we felt other countries all had colleges but we couldn't call it a college because of the Royal Colleges. There was a precedent in America with the Academy of Psychosomatic Medicine, so we went for that but clearly to the British ear that didn't sound very well and that name soon changed. Fortunately we didn't have to change the initials. It was still BAP.

How useful was it to have Max Hamilton on board?
Oh he was absolutely invaluable because his name was very important. You couldn't possibly have founded something like this without including him and he was very very good in the early days. He was very good in controlling meetings. The inaugural meeting was noisy.

Do you want to go into that in a bit more detail. There were a few meetings between the first one in June and then the two meetings on 22 and 23 November.
Yes my memory of the initial opening meeting is perhaps not all that clear but there was a lot of dissension at that meeting. Firstly from some basic scientists there, obviously because they hadn't been included but also from representatives from the pharmaceutical industry. They took great exception because in the founding letter that was published I had said something about relations with the pharmaceutical industry and their argument was that they were

psychopharmacologists like any of the rest of us. They argued that we were discriminating against them. But of course the reason for that was this background that had happened at the ACNP. But all of those things got smoothed out. Max Hamilton in fact smoothed it all over and everything then was set up I think to most people's satisfaction. Philip Bradley was brought into it..

later on they were all brought in....
I don't know if they were all brought in at that meeting because at that meeting we only had a Steering Committee, we weren't a formally elected Council at that time. It was at a later meeting where we actually had an election - and I remember thinking, I was sitting up on the platform with Max Hamilton, and I said well all this effort I've put in and perhaps now I won't get elected. But I was and I think George Beaumont was elected assistant secretary. We had two secretaries originally, a principal secretary and an assistant secretary. We then set up various sub-comittees, most important of which was the programme committee and the programme committee appointed their own meeting's secretary. Well as time went on it was clear that the meeting's secretary was really the most important person because he would be responsible for the whole programme of what we did but in point of fact, that person wasn't actually an elected officer.

Anyway we set out with Max Hamilton, as Chairman and President and I was the secretary. I in fact had arranged most of the early meetings, including the first clinical meeting we ever had at the Royal Society of Medicine - on Stress and the Heart. I got various contributors to come and speak at that meeting. I remember very vividly Max Hamilton insisting that the membership fee should be £10 and in those days a lot of people felt that was too high but he said "no, if we put it at that level then we won't have to increase it". I don't think it was increased for about 10 years, which again was showing his very good commonsense. Merton Sandler became involved at a very early stage and he organised a meeting which clearly was mainly concerned with the laboratory side of things.

In terms of office in those days you spent 3 years on Council then you went off for a year and if you were re-elected back you could be, but you had to go off for a year. Except of course for the immediate Past President. The President served 2 years and then became immediate Past President and there was also a Vice President who was the President-elect. But of course the problem was that we had all started together and were due to go off together after a 3 year period and there was not enough continuity and that was when I think the "disastrous RSM meeting", referred to by George Beaumont, occured.

I didn't know about a disastrous RSM meeting.
I don't know what happened. They didn't get any advertising and it floundered rather. It was after that that Merton Sandler became President. He was the third or fourth President. At that point, I believe, George Beaumont was the programme secretary. He was absolutely invaluable to the Association because he drafted the Constitution and that was a major contribution.

It was he who drew up the Constitution rather than Max Hamilton
No, it was George Beaumont but he only served a year I think as programme secretary and he then resigned. I remember Merton Sandler phoning me and saying look we haven't got a programme secretary; could you come back as programme secretary? I agreed to do this. Although I had been very much involved in the foundation, this was really the period that I

enjoyed the most because I was organising all the meetings. It was really what I had wanted to do from the word go. And I think we never looked back after that. But it was Merton Sandler, who pulled it all together. He knew everybody.

We then had a routine summer meeting which would be held two out of three outside London and two other meetings which were 1 day meetings, one in the spring and one in the autumn. Merton arranged for us to hold those meetings at the Royal Society, which is really a much nicer place than the Royal Society of Medicine. And he gave me really a very free hand. I organised a meeting at Exeter University and three of the BAP monograph meetings.

Some of our early publications were through Raven Press again because of Merton Sandler. When Oxford turned them down, he said why don't you go to Raven. Stress and the Heart written 13 years ago is still selling. It badly needs a third edition but I haven't the time to do it. Then there were another 2 that came from organised symposia. These were all half day symposia which are not enough for a proper book. So I invited extra contributors from outside to cover the whole subject. So, as I say I was then very much involved in the management of the meetings. One was in Aberystwyth - I always remember that one.

Aberystwyth? who did you expect to go.
Well it was a very well attended meeting. There were over a 100 people there. That was Philip Bradley's suggestion. I think he was President. He suggested Aberystwyth. Nobody knew anything about it and I remember going on a trip to see what facilities there were and they were good so the meeting was set up. I think it was on a Monday, Tuesday and Wednesday. But what nobody told me and I didn't find out, there was no train service there on a Sunday so how people got there I have no idea. I know somebody actually hired a helicopter and flew in by helicopter. We had 10 pharmaceutical companies and they paid £250 each to exhibit which paid for the meeting - dinner and everything. That was what I used to do for the annual meetings. For the 1 day meetings in the spring and the autumn, I would approach one company but never the same one twice in a row and ask: would you sponsor this meeting and that paid for those meetings too. So, we started off on really a good financial basis and I think it's gone on from strength to strength.

The other thing was was that nobody realised that Aberystwyth was "dry" on a Sunday. However other means were found of circumventing that and the meeting went extremely well. Another one in Exeter also went extremely well and the third one I did I think was the one in Birmingham which had already been more or less set up by Merton and Phillip Bradley and I never had very much to do with that.

When it came to the end of my 3 year term and they asked me if I'd like to be the Treasurer, I didn't want to very much - I had other interests by then. So I really dropped out of things from thereon. I used to go to the meetings, but over the years I've tended to attend less and less. Just like the CINP, they tended to get dominated by the basic scientists. I'm afraid this is the tendency - clinicians unfortunately have responsibilities to their patients and can't always get to meetings. Basic scientists it seems are always able to. And I think that is a pity. So over the years I've tended to be less and less involved with the BAP.

Why was Merton Sandler so important. Do you want to expand on that a bit more?
Yes he was responsible for re-galvanising it. I've found that this happens with so many organisations, with societies and so on. The initial enthusiasm is usually carried on - in this

case only for the first 3 years because all the founding members were on the Council for that time. When they go off there is a hiatus for a period and that is a very dangerous period because the organisation can founder completely. I think that we were in danger of doing that. But Merton really took the reins. He's a very good delegator and I think he was really responsible for inspiring people. He didn't actually do a great deal unless it was necessary. If somebody was supposed to do something and didn't do it then he would do it himself. He would prefer to delegate but he chose the right people to delegate to. And he was invaluable if you were stuck for speakers. I knew clinical speakers but didn't know basic science speakers but he just knows everybody in his own sphere or not. So I think that was really a turning point and I don't know what would have happened if..

Knowing Merton I'm sure he brought a certain humour to the proceedings. **For a long time during the 1980's the BAP was a fun group and it has always seemed to me that a great deal of that stemmed from Merton**.
Oh yes it was. But that was how we had started. We used to have our Council meetings, I think once a month when we were setting it up, at the RSM - we had a private room there. I used to arrange the food and I went along and saw the catering manager and asked if he could improve on the standard buffet - so we always had cold duck and we used to sit around then, help ourselves and eat while we were talking and there was a very good feeling - everybody was full of enthusiasm. As the group broke up it didn't always continue. Anthony Horden had really been responsible with me in setting it up but lost interest and went off to Australia.

As you say you went to the BAP meeting this year and it was very much basic scientists, why do you think that is because clearly the primary use of psychotropic drugs is in general practice. What can be done to bring this element of psychopharmacology back on board - at the moment the only GPs involved are yourself and George Beaumont,
Exactly and you will find that I put this in the original objectives that we would envisage our membership would consist of basic scientists, psychiatrists, psychologists and various other categories. General practitioners were also in fact included. Many years after one of the popular journals phoned me up and said they were looking at this and wondered what the contribution of the GP was - how many GP members did we actually get. The answer was we didn't get any, other than George Beaumont and myself.

The reason for that? Well GPs are very busy for one thing. They don't have the time to come to meetings and of course psychopharmacology is only a small part of their work and there is a certain lack of realisation of its importance; in particular, in relation to, the affective disorders. I find even now I'll get patients referred to me with depression and they say I went to my GP and he told me just to shake it off and refused to give drug treatment. So clearly there is a need I think for better education for general practitioners particularly in the area of depression. Anthony Hordern used to say that suicide is the mortality of depression and he was right.

What can be done about the lack of GP involvement ?
I don't know what the present constitution of the council is or what is recommended but in one of the early minutes you will probably see that it was decided that there should be an equal representation between basic and clinical branches and also that the presidency should alternate between a clinician one year and a basic scientist the next. I would have thought a GP could be brought in in some way like this. I am not sure whether the Presidency still alternates like that or not.

It has done, but that caused some fuss when it came to Philip Bradley's turn to take over the presidency.
Yes it did. It was the only time when we had an alternative candidate and an election. The arrangement had been that we would recommend a candidate. I remember it very well because if there were counter-nominations they had to be in 3 weeks before the actual meeting when the election would be made. There very seldom were but on that occasion Merton certainly was one. Philip Bradley was the nominee of Council and Merton must have been nominated by somebody else but they always got on very well with each other. I'm not really quite sure why an election happened at all.

One more meeting that you were actually involved in, generated a great deal of fuss - that was the Guernsey meeting.
The Guernsey meeting - yes well I was surprised to read what George Beaumont had written about that meeting. To begin with it wasn't the first meeting that was held abroad. One had been held in Paris a year or two before - Mike Trimble was the secretary then; it was a joint meeting with a French organisation. There was a comment that it was too expensive for people to go but I was puzzled by that because I went to the meeting and I thought it was a jolly good meeting. It was very well attended, the hotel was full and some people had to stay outside.

The issue there was that the basic people were saying well it's all very well drug companies taking clinical people to plush venues but basic scientists won't be able to be involved if that's the way things go
I'm not sure that is the case. Maybe it was then but I don't know. I wasn't officially involved at that stage but from my point of view I appreciated that meeting very much because they made Max Hamilton and myself honorary members for life, which is the highest honour the Association can give. We were the first two British - I think they made people from abroad and there were about 10 honorary members and we were the first 2 British clinicians to be made honorary members. So I enjoyed the meeting very much but also I helped organise a symposium - something to do with sex.

Sex was a very unusual thing to organise meetings about 10 - 15 years ago.
Yes that's true, but there you are. It's an important subject.

Well yes clearly but George in his interview was saying that when he began to get these reports about clomipramine and made something of them, the company weren't keen for him to discuss it in public
No, quite. These days I'm sure they would be but I also remember one of the spring or autumn meetings at which we had Patricia Gillen speaking. She was working at The Maudsley, which had a sex clinic in those days which she ran. Some of the slides she showed didn't leave anything to the imagination. And I always remember this meeting was held at the Royal Society, and she was up on the stage and I was chairing it and the lights were half down and she had one of these slides up showing some esoteric position and Max Hamilton came in and sort of peered round, blinking a bit and looking at the screen he was absolutely transfixed. So, as I say they were rather fun the meetings in those days.

Taking you back to the RSM meetings, some of the other themes that appeared to come up were the issues of why are we having this group? - the argument that if you're

interested in pharmacology you should join the British Pharmacological Society and if you're interested in biochemistry you should join the Biochemical Society and so on. Do you want to comment on that. The idea that this wouldn't be a proper scientific organisation - it would be a mongrel organisation.
There were very good precedents for us setting it up. There was an American College, there was the International College which had been going for some considerable time. There were Czech, Scandinavian, German and there was even a Turkish College. So other countries were setting up organisations in this particular discipline and of course the main precedent was the CINP itself which had been going for about 10 years or more. So clearly if there was an international organisation devoted to this speciality and other countries have national organisations it was about time we joined the bandwagon and indeed we should be in the fore-front of developing this very important speciality. This was our feeling so I don't think those objections ever came to very much. They certainly didn't impress us.

What about the feelings of exclusion on the part of the basic scientists - in a sense they had their own organisation - the Brain Research Group, so the impetus to form a BAP wouldn't have been there in a sense
Oh no..and they were well catered for by the CINP. So no, there was little impetus from that direction. Initially, it was purely clinicians. I myself was involved in clinical work and I didn't realise how much relevant basic science work was being done - and of course there were very important contributions. However, sometimes the clinical implications of some of the work, that is when I could understand it, escapes me.

So do you think the BAP has lost its way? For instance, should there be more prescribers, especially perhaps GPs, because after all it is GPs who actually prescribe these drugs more than anyone else and actually these days they also do more clinical trials on psychotropic drugs than anyone else.
This is very very true. As I say I was involved in this at a very early stage, even before George Beaumont. In 1958 in fact I set up The General Practitioner Research Group, which I've described in The Practitioner, which also carried many of our early trial reports. At that time I had an arrangement with The Practitioner - W A R Thompson ran it from this lovely office in Bentinck Street which had a circular lift, I hadn't seen a circular lift before, and I think it was owned by the Financial Times at that time. We had a regular slot in The Practitioner which was called General Practitioner Clinical Trials section. In every months issue we had one or two of our trial reports and that went on for many years.

Why were you so keen to get involved in that area so early. Clinical trials really only began in the late 50's so it was very early to be talking about a clinical trials group..
I'll tell you how it started. I was in general practice but I never really cared much about general practice - I had gone into it for a living. But as I continued I became more and more interested in the use of drugs and when I saw an advertisement from Menley and James, which was a drug company in those days - it was later taken over by Smith, Kline and French - for a part time General Practice Advisor, I applied. Now the reason for that was that they were just bringing in oral penicillin preparations in a mixture form for children. The main use of oral penicillin was for children but they had a great problem disguising the taste of it. It's not much good having a preparation if a child spits it out. And so they wanted a general practitioner advisor. I tried out lots of preparations in my own practice and that extended then to other drugs. I even got my first trip to the States under their auspices. I remember travelling on a wonderful plane called a StratoCruiser which had 4 propellers and it took 12 hours coming

back which was faster than going out and it was all first class. It had 2 decks with a bar down below and then you slept in what is now the luggage rack.

Anyway Kenneth Carter their medical director transferred to Ames, and I followed him although of course they were mainly into urine testing strips. They didn't have many drugs. I was their part time advisor for quite a while - it involved one day a week that's all but after a while I felt well how on earth can I branch out of this. So I conceived the idea that the limits on what I could do were that I didn't see enough patients to do a proper trial. So I felt well lets get a few people together and then approach several firms. I wrote around to old friends, most of whom I had known at Guys. I got a nucleus of 12 and I then approached 4 companies. Of the companies I chose 2 large ones and 2 small ones; the 2 small ones didn't have a medical director but they were glad of advice as well. I think Ciba was one, Pfizer was one and one of the two small ones was Bengue, they are probably no longer in existence but they had a number of products as well as a well-known balsam. The other one was Camden Chemicals, who made lithium. Anyway they all came in and immediately started giving us all sorts of drugs to try out. Of course in those days there were no regulations about at all. It was just a matter of handing it out to the patients - here's the latest thing! We didn't really think about side effects.

Were these all drugs or just psychotropic drugs.
No, all drugs. I was still in general practice then. My interest in psychotropic drugs came about shortly after this. Kenneth Carter was a good friend, who although I think he disappoved of my leaving Ames, when I had a trip to the States, phoned me up. He said: "by the way I was talking to some people down in Washington and they are very interested in the idea of your general practitioner research group; Jonathan Cole of the Psychopharmacology Research Service is interested. I was telling him about your work with general practitioners and he said if you'd like to go and see him they'll pay your flight from New York and your expenses there". I'd never seen Washington and thought it was a good chance to see it. I didn't have a particular interest in psychopharmacology then. But I remember this meeting clearly. I remember people like Mitch Balter, who was one of the people present, and as the meeting went on somebody said "now when you apply for one of our grants, here is what you should do". I remember feeling quite amazed at the idea but I thought "that's a jolly good idea" and so I did...

This was when?
It would be around about the early 60's because the group hadn't been going all that long. So, anyway I applied for one of these grants and I got it. In those days they had a lot of money to give grants in psychiatry and they didn't know quite what to do with it - at least that's what I was told. And somebody else said, when I asked why did Jonathan Cole choose me, that "well he's a guy who plays hunches and you were one of his hunches". I think the main reason was that it was quite impossible to do any drug trial in the States with general practitioners. They just weren't interested. They all earn so much money anyway, so they felt well here's someone doing them. It was a wonderful 12 years I had. I was the only foreign grant holder. The original organisation was the ECDEU, Early Clinical Drug Evaluation Unit, which is now the NCDEU. Each year there was a meeting and that consisted of all the investigators who had grants and we numbered 24. And I was the only one other than Lehmann and Ban from Canada who was not American. It was very nice. We used to get together once a year, initially in Washington but it moved to Key Biscayne, which was even better. Those were my 2 meetings, ECDEU at the end of May and ACNP in Puerto Rico in December - who could wish for anything better than that. They were lovely meetings because they were relatively small,

particularly the NCDEU. I got very friendly with all the American investigators and this was very pleasant.

Who were the key people in the US at this point?
George Simpson, who worked with Nate Kline, Jonathan Cole and then his successor at NIMH, Jerry Levine, as well as Mitch Balter, Martin Katz and Ronnie Lipman. There were a number of people involved who had played a part in developing rating scales such as Al Raskin and Lino Covi at John Hopkins, Leo Hollister in LA and John Overall from Houston who put together the BPRS. There was William Zung of the Zung self rating scale and of course Donald Klein, Karl Rickels and Ronald Fieve. There was Heinz Lehman and Tom Ban from Montreal. There was always a strong representation from psychologists. In America psychologists were doing all the ratings - Richard Wittenborn from Rutgers I remember..

What do you mean they were doing all the ratings?
They were actually rating patients. These were often done by psychologists and they would do a lot of the design of clinical trials and virtually all the statistical analysis so there was a very strong influence from PhD's but no influence at all from basic scientists. It was always clinical and I think ACNP was the same, certainly in my time. There was very little, if any, basic science in it which is probably another thing which influenced my interest to model BAP on the ACNP example.

So it was under Jonathan Cole's influence that you moved from just being a GP in a general drugs group to being a GP interested in psychotropic drugs.
Yes that started my interest and as I got more and more involved, of course I became fascinated by it and our General Practitioner Research Group, which by that time had grown - at one time I had 500 GPs all over the country doing clinical trials.

An organisational feat that ! How did you manage it?
It was and it was all run by myself with one secretary but she was very good. There were no computers in those days, no calculators even. I remember getting an early statistical calculator which was invaluable but it cost a fortune. I think it was just methodology really. Everything was done with pre-printed letters or my secretary would call up the GPs. But anyway I then formed a sub-section of the General Practitioner Research Group which was the Psychopharmacology Research Group and that consisted of members who had a particular interest to do psychotropic drug trials. Now of course they became more and more expert as time went on, but at that time we didn't have meetings or anything else. It would have been impossible with that number.

On that point, were you using any inter-rater reliability assessments and all that ?.
No. We just presented the rating scales to the investigators and said fill them in. I have to give George Beaumont credit there for starting protocol meetings and having video tapes and really checking inter-rater reliability. No, we just muddled on - which was really what everybody else was doing. Even in the States they weren't doing inter-rater reliability. It all came later.

Again my aim was to do everything as easily as possible. We had a punch card but because I really didn't want to waste time and money on printing punch cards they used to be mimeographed. There were no photocopiers in those days but I had a local agency who could produce these - on foolscap sheets. I remember Jon Cole saying at one meeting "Dr Wheatley uses the largest punch card I have ever seen". The answers to the questions were put

against a punched hole so all the investigator had to do was make a mark - they didn't have to write very much at all. And so that was what we used. Then of course you needed to collect very little data in those days. If we needed more data, we used more than one card but then analysis became more difficult. But by that time pharmaceutical companies were tending to do their own analysis of the data although I have always tried wherever possible to do my own analysis.

Now of course clinical trials aren't just run by the companies but they are run by the companies in various different parts of the world, so no-one owns them in a way I guess you owned your trials.
Exactly, and a lot of companies tend to only pay lip service to the pharmaceutical associations' guidelines, particularly the section that companies should encourage publication even of negative results, while reserving the right to ask the investigator to discuss their report with them or something like that. The last time I was involved in this way there was a little dissension over a study, a few years back. That was a multicentre study. My group contributed 150 patients to this trial which was an appreciable contribution. When it came to an end, I had done my own analysis and written my own report which I always sent to the company so if they had any objection to it they would come back to me. And they came back and said "well we've decided not to go ahead with the drug because we had an adverse report from one hospital but certainly go ahead and publish what you like". So I went ahead and published it but meanwhile they had a re-think on this and without really consulting me at all, had written up all the results, putting my name on as a co-author on something I hadn't then seen. Then my report appeared in print and they were annoyed about this saying well we didn't know you had actually submitted it - you should have let us see the final version. But they had seen my report and I said my submission to a journal was based on that report. They have a habit of changing the text which I don't like - I'm not going to have my English changed around into phraseology which I would never use. Someone, I can't remember who it was, said that I was a disgrace, I had let my colleagues down and this, that and the other. But they didn't have a leg to stand on because I had, in fact, strictly observed everything that was in the contract.

But that was the last time I did it because now one's only such a small cog. We're doing a trial on Alzheimer's disease here - an enormous, multi-national study. I enjoy doing it because even though it's double blind, I think the drug is working and I think I can pick up patients who are responding. But the documentation is vast for just one patient. There are other trials I am doing here - they're on antidepressants and a hypnotic coming up. These are just bread and butter although I hate filling in all these forms. I enjoy doing things like Hamilton Ratings but I sometimes find the monitoring visits somewhat tedious. Anyway I appreciate if you're going to do clinical trials you have to do this. But I try to keep individual research going particularly in the psychopharmacology of sleep. I was the first, in this country, to publish reports on the clinical use of both zopiclone and zolpidem. Zopiclone was in the British Journal of Psychiatry and I presented zolpidem at one of the NCDEU meetings.

I'm trying to do further work on sleep. At the moment I'm particularly interested in sleep in patients with HIV. I've been studying HIV patients for the last 6 years, at an AIDS Centre in Crouch End. I've got no support for this one whatsoever. What I want to do is some polysomnography on these patients and now through the good offices of Chris Idzikowski I have a loan of an Oxford portable machine and he's doing the analysis free of charge. We plan to do them on half a dozen cases and it looks promising - we are doing our 4th one on Tuesday. My only expense is to pay the technician - she has to come over from Wimbledon.

I've tried to get a grant and I've been promised one but it hasn't materialised. I'll pay for that out of my own pocket because I make enough out of the other trials to indulge my hobby if you like.

What are you hoping to show?
A very good question. I'm particularly interested in sleep staging and especially deep sleep because there is no doubt deep sleep is a stage of sleep in which changes take place in the body, whether they are concerned with repair or what is less clear but it is certainly a very essential part of sleep. This clearly raises the question of what drugs might be helpful, because you don't want to use the benzodiazepines, which increase sleep by increasing the light stages, in somebody who is already immuno-compromised.

But to advocate anything what you've got to show in the first place is that people with HIV in fact have sleep problems - that's been done. We've studied a group of 45 HIV positive patients and 45 matched controls, matched for age within 5 year limits and sex, because they are mostly male - there are 3 females out of that group. And in fact clinically, using a simple clinical scale asking how they've slept there is greater impairment of sleep in patients with HIV and much greater in fact if they've actually got AIDs. So the next step is to do sleep EEGs and see how this correlates clinically. And as I say, we've done 3 patients and the results so far have been interesting.

The problem is to try and get funding. I tried to get an NIMH grant. At that time I had no access to AIDS patients here because I didn't know about Crouch End and obviously all the big centres have got their own programmes and they're not interested in somebody who's got no experience with AIDS. But I got in touch with David Sheahan in Tampa who is Professor of Psychiatry there and he was very interested and it occurred to me that perhaps they would have AIDS patients and he said "yes we do but nobody wants to know them - come over here and treat as many as you like and people will say thank you very much". So I went over there a few times and in fact I still have a work permit to work there. And we put in a grant application, or rather I did. Because of the possibility of plagiarism, I had to disguise the main objectives and make it much more general and inevitably it got turned down.

Listening to you talk, what I am struck by is the fact that quite a few of those who were involved, in the early days, this has come through in a number of interviews, had such a range of interests. These days psychopharmacologists, like everyone else are often forced to be one issue people, whereas you're clearly not a one issue person.
No. I'm interested in ideas and I pursue my ideas. What I am hoping is that if these EEG traces do show that HIV patients who are having sleep problems have a deep sleep problem then it will be an inducement to try and get some financial support. If I could set up a sleep laboratory here, then we could buy our own machine which would be the main expense.

The other thing that interests me is that you are very entrepreneurial. Why have you broken the mould so often?.
I don't know. I have always liked to do something different. That's just the way I am . I think I've never been one to go along with the herd. I like to do my own thing. I like to do it, if you like, with advice from other people but not really at the behest of other people. The beauty of the grant that I had from NIMH was that they gave me an open brief. They said David you do whatever you like, we'd just like you to tell us what comes out of it. They would send me money and I would say "we'll do this trial".

I was interested at one time in the use of tranquillizers and coronary heart disease - this was before benzodiazepines came under a cloud and we did some double blind studies to compare diazepam with a placebo added to standard cardiac therapy and I just did it. Someone would make a suggestion and say look this might be an idea but there was no veto over it which was what I liked about it. Of course in the early days there were no ethical committees although towards the end of the 12 years I had to set up an ethical committee and use them

That was I guess in order for the data to be used for regulatory purposes ?
Not under the grant. Nothing to do with regulations - that was the job of the pharmaceutical companies. I was just doing research. I obviously needed to get supplies of drugs from companies so the 2 things might be combined but..

So you weren't so much only doing trials on new agents as doing interesting trials on anything that were in the field.
Yes for instance Arthur Prange wrote a couple of articles on thyroid hormone potentiation of tricyclics. He was a very good friend of mine. He was very keen to get confirmation and he asked me if I could do a study with my GPs which I did. Now in order to do that I had to get triiodothyronine from Glaxo I think. I remember writing to Glaxo asking could you supply me with this and in those days if you asked for something like that from a company they would do it out of good will. And they wrote back and said well - they obviously didn't want to do it you see - and they said well we can supply you with placebos but you'll have to pay for them. So I said oh that's all right I have funds to pay, which I did. They never in fact charged me, so they did supply me. That was one study which I did. The benzodiazepines after heart attacks was another but in the end I couldn't pursue that which was a great pity because the clouds started to descend on the benzos.

You've raised a number of issues there to do with how things have changed in recent years in terms of pharmaceutical companies and the way they interact with researchers. They have necessarily become much more bureaucratic because of the CSM, the FDA and all the regulations of various sorts - has the weight of regulation begun to poison the goose that lays the golden egg. Even if they wish to be, companies are not as able to be as freely co- operative as they once were.
No they can't and it's a problem clinically. There's been an enormous change and I think it's gone too far the other way really because now the complexity of drug trials and all the checks and so on really make for inaccuracy. The documentation of this trial I'm doing with Alzheimer's is pedantic. An initial interview with the patient takes about 5 hours and they are also seen by a psychologist and then by a general physician - in other words about a day and we each have a volume to fill in. If I make any alterations, the alterations must be initialled with the date even if I have just written a 7 and changed it to an 8. That won't do it's got to be crossed out and re-written. The other thing is that some of the sections have a space for comments but comments have to be written in capital letters because they are going outside the country for analysis and maybe they can't read my handwriting. This is the sort of totally unnecessary workload that is being put on clinicians and it's bound to interfere with your clinical judgements.

In my view it's defeating the purpose of the exercise and quite unnecessary. Really what I think pharmaceutical companies should be doing, if they really want accuracy, is take all this tedious drudgery away from the skilled clinical investigator who should be giving much more

attention to the assessments he is making because clearly in conditions like Alzheimer's for example, the assessments depend very much on your clinical impressions.

To an extent we are becoming deskilled then. What you are saying is that the companies want to standardise things so much, there will be no room for the creative clinical impressions that have proved so important in the past
Exactly. In other words they are trying to make a precision machine out of what still remains an inexact science.

One more name which comes up in the clinical trial area was Linford Rees. Reading round and having had the opportunity to talk to him it seems that in the late 50's or thereabouts, as I say clinical trials were new around that point, there were only a few people who really understood them in psychiatry in this country, such as Max Hamilton and Linford Rees. But he never became so heavily involved in the BAP
Yes I'm not quite sure why not. He was a great friend of Anthony Horden and Anthony was a great admirer of his and may I think have mentioned his name as the first president but perhaps he declined because he was very busy at the time. I would look upon him as a sort of a diplomat. He was a wonderful diplomat as well as being a very good clinician.

What about the MRC trials
Oh yes well the one I think of is the one which purported to show that there was just a tranquillizing effect to antidepressants. That was something which I thought we would try and duplicate in one of our early trials. Edward Hare was the guy who was involved in that. He was then editor of the British Journal of Psychiatry.

Yes I had actually forgotten about that because the early editors of the British Journal of Psychiatry, Slater and Hare, while biologically orientated really have not been drug oriented.
No that's very true. I remember what we did. I wanted to find out whether it might just be a sedative effect so what I did was to look at the number of trials we had done and look at the proportions of patients who complained of sedation and then compare the outcome with the drugs and see whether those who were sedated got better quicker. I think that was published in the British Journal of Psychiatry.

Another suggestion of the NIMH was that we should look upon doctors' attitudes and that gave me one of the very few papers which I got into The Lancet . We classified doctors as to whether their attitude to each individual patient was optimistic, indifferent or pessimistic as to whether they were going to respond to a particular drug. Now this is compounded obviously in the case of a particular patient of what one knows about the patient and whether they ever respond to anything and also there's the belief about whether the drug is effective or not. The patient would be assessed in the same manner.

In anxiety there was a very clear cut distinction from depression. In anxiety expectations of treatment made a big difference. Optimistic doctor/patient relationships did much better than pessimistic ones but in depression you didn't get that relationship at all. At that time a lot of people were saying well you can treat depressed patients as well with psychotherapies as with drugs. But this study pretty well demonstrated that in general practice anyway, the attitude of the doctor wouldn't make any difference. Anxiety yes, depression no. So that was something we did with NIMH which had been suggested by them. They did come up with some very good

ideas sometimes but it was up to me whether I liked their idea. I found that a very nice way to work.

Stress is another area you've been one of the first into which has again become very fashionable. Did you anticipate it becoming fashionable again.
Yes indeed. When I became interested in it, I was a bit disconcerted at the sort of people who were practising "stress therapy" of various kinds. They often seemed to be people without any qualifications at all. And I felt there was a need to put it on a more scientific basis. I suppose my interest started with that book Stress and the Heart in 1977. I was interested then in the effects on the heart because cardiology has been my second love if you like after psychiatry and it was my first love until I met psychiatry, or psychopharmacology. So I did have that interest in the effect of the mind on the heart and then I felt well what do you mean by stress. I had asked Hans Selye to write the opening chapters of the book. I used to go and see all my authors so I went to see Selye when he was alive and..

What was he like?
He was a funny little man, sitting in this great high back chair. You'd go down this great corridor with signed pictures of Winston Churchill, De Gaulle and every world leader who had been to see him or sent congratulations to him. He was very pleasant and said yes of course he would write an introduction which was great. But there again I read his books and I wasn't really awfully clear of the clinical implications of a lot of his work. I think I felt there was a need to try and define exactly what stress is and how we measure it and to set up a stress clinic.

Malcolm Lader has been a very good friend indeed to me. When I tried to set up a stress clinic in order to do this, I tried a number of hospitals, I had tried Guy's and Charing Cross and the initial reaction was always very poor. I think Malcolm Lader was my last resort and Malcolm said what a good idea, lets go and talk to the Dean and so it was set up at the Maudsley.

Then I had to devise an instrument to measure stress. After a lot of thinking I decided there were 9 areas which I would try to measure including social habits, such as smoking, drinking, use of drugs, caffeine containing drinks, then social relationships, which include personal relationships, stress at work, stress in the home. Then came life events, things that have happened in the past which are still causing stress in the present. Then I had a section on sexual stresses which was concerned with aspects of sex, especially libido and whether the individual is satisfied with it, whether they felt they were over-sexed or under-sexed in relation to their partner. That and different physical aspects, such as anorgasmia in a woman, premature ejaculation and so on, and then the psychological aspects of the actual techniques of love making. People are only too pleased to talk about this - very very frankly too. Then there is masturbation and feelings of guilt over masturbation. The other areas covered are psychiatric disorders, a section on sleep, a section on menstrual stress for women, the peculiar stresses of old age and inevitably a section on stress and the heart. You've got measurements there - you can measure the heart rate, blood pressure and see if they change when hopefully you relieve the stress problem.

Each of the individual items are scored on defined scales so that you can make a score on each. I just called it the stress profile to begin with but then I thought, well I might as well be known for something so I called it the Wheatley Stress Profile (Wheatley 1993). It has generated quite a lot of interest. I think the main finding when I studied 300 patients at The Maudsley was the very high incidence of depression as a sequela of long continuing chronic

stress. Stress that could not be avoided such as a person you hated at work but you couldn't do anything about it because you daren't lose your job. One woman she came in and she was 87 and she said the trouble is my husband - I can't make up my mind whether to leave him or not. I said well how long has this being going on. And she said oh, ever since we got married. I think in the end she did decide to leave him and she did leave. Depression is important because it is something you can treat, because the more depressed a person becomes the less able they are to cope with their stress problems and antidepressant treatment really is very very effective. The minute you can relieve their depression then they say I don't know why I put up with this all this time, I'm going to divorce my wife or whatever the problem might have been or I'm going to change my job.

So, that was how I started the clinic and this went very well and I got quite a few publications. In particular I did a study with Dr Ji Jianlin in China . There is also a hospital in America where they use it. I shall be presenting a paper on that at the World Stress Congress in Washington in October. It has been translated into Spanish and into Japanese.

The issue of stress leads on to the question of the minor tranquillizers and your book The Anxiolytic Jungle, do you want to comment on the impact of all those controversies on psychopharmacology generally?

Well I'm not going to speculate on that one. I have my own ideas as to what may be behind all the fuss. Just we might say this that a kind of climate has been created in this country which has made people very suspicious. Obviously we had to pay heed to the question of dependence but the way things have developed has made life very very difficult. When I first started the clinic I was prescribing tranquillizers but I very quickly found out that there was a lot of resistance from patients and I very quickly had to stop it.

So what do you give them. They're not all depressed. I have patients with panic disorder, for example, obsessive compulsive disorder and just generalised anxiety. In some cases propranolol helps - that was another early study I did - it can sometimes help the panic attacks for musicians and so on. So what do you use. There isn't anything. I don't know whether there are any non-benzodiazepine tranqullizers in the pipeline. I think there is a need for them, there's no question about it. I personally will go on prescribing benzodiazepines because according to the main expert Malcolm Lader, it's only 20% of people who are likely to become dependent. It means that 80% won't. But you need long term treatment, short term treatment, say confined to 4 weeks, is not much good really. And since benzodiazepines don't cause any other major side effects it's only dependence thats a problem - any evidence from over-dosage shows that suicide is very doubtful, compared with other drugs.

What would happen do you think if we had a blood test that would pick out the people, who would be likely to become dependent

It would be an absolute godsend. The restraining factors are the medico-legal implications of it. You're scared to. And I very quickly stopped doing it at The Maudsley.

Related to this issue is the growing involvment of the media and the law had come in psychopharmacology. Up til then the benzodiazepine saga, psychopharmacology was just something for clinicians and basic scientists but now there are a lot of other stakeholders.

Well I think it's part of the whole change of attitude generally towards the medical profession. We live in a era of doubt and uncertainty, whereas when I started in practice you were the authority figure and nobody would ever think to question any opinions that a doctor made or

any drug. If you gave a drug, the side effects had no publicity even if they were appreciated. It was thalidomide really blew the lid on it. People certainly realised then that drugs can be dangerous and clearly that's a theme of great attraction to the media, who have been dining out on it ever since.

I quite often now get people who are severely depressed to whom I give an explanation of the biochemical cause of depression, exactly what the antidepressant drug does - its not a tranquillizer you won't become hooked on it - it corrects a chemical abnormality. A bit simplistic maybe but they do work provided the patient continues taking them but I still get this "I don't want to take any drugs". I shrug my shoulders and say "well what else is there?" Usually people do come back and they take them and they get better. So unfortunatley the controversy over tranquillizers and benzodiazepines in particular has clouded I think the whole area of psychotropic drugs being prescribed in that people think that anything psychotropic is going to produce dependence or addiction, or that in some way the drugs are "taking over their minds".

This is partly responsible but it's part of the general, I think, increased awareness of the public that medicine is not as perfect as we once thought it was, that some illnesses cannot be cured and that some drugs produce serious side effects, which was glossed over before even when it was actually known. And the media want sensationalism - anything so mundane as the number of depressed patients who are saved from suicide is not of interest. But the one patient who takes an overdose and has a cardiac arrest - it immediately has to be somebody's fault; whose fault ? It must have been a negligent doctor or its the medical profession itself or of course the pharmaceutical industry. And then there is this enormous growth of paramedical procedures and fringe medicine and so on - you can't really blame the general public if they are not getting relief from standard medical treatment. They need to get relief, there's no good telling them there's no scientific basis for homeopathy, they will just try anything. And unfortunately some people seem to make claims which we in the medical profession would be wary of making.

Picking up the issue of the industry. When you wrote the letter proposing the establishement of the BAP, as you say there was concern to have a policy as regards the industry. It seems to me that in the UK perhaps more than in Europe and more than in US we've been very wary of the industry, why is this?
That is very very true. I think it all stems from the thalidomide affair. This was a shock, not only to the general public but certainly to the practising clinical profession too. I think up to then we had complete faith in any new drug that came along and serious side effects were not reported or they were not associated with the drugs and I would certainly say that any new drug that came along, the very fact that it had been marketed meant that it was safe. I took many things myself but since then I'm much more wary about taking things. I think an education after all has happened about drugs and their effects and their disadvantages as well as their advantages and that's progress.

It's just that you can progress too far sometimes I think without weighing up the other side of the picture. The other side of the picture clearly being the morbidity or even the mortality caused by the illness itself. This emphasises the role of the doctor as the person who has to make that decision - whether the treatment I'm using now will do my patient more harm than the illness if I leave it untreated and I often quote that when I'm talking about sleep and sleep

disorders. Because some of the adverse effects of chronic insomnia are far worse than any possible problem you might produce with a benzodiazepine.

Can I chase further the question of the responsibility of the BAP to educate the public. It seems to me that there's something about educating public perception of risk that we're falling down on - we're leaving the public to be influenced by programmes on TV or whatever.

I couldn't agree more. It was felt, in the early days that by holding our meetings and generally improving standards we were in a sense informing the public. But these days that is certainly something that we could turn our attention to. We could organise an open meeting, to which the public could come. Now there's a very good precedent for this which is the Edinburgh Science Festival, which is now in its 4th or 5th year. This is open to anybody who wants to go - they run the whole range of meetings concerned with science and it goes on for 2 weeks and there are all sorts of exhibitions and so on. The public pays to come in but a very modest entrance fee, £1 or £2 per session. I've been involved in the last 2. The first one was a session on stress and it was packed to overflowing and there was enormous interest from the public. There were the speakers who were able to answer any questions on the spot and if they had more publicity and perhaps a publication on it, it would be even more helpful. Last year I did 2, one on depression and one on sleep and again both meetings were sold out and people had to be turned away. The topics had such general interest and one was able to put them in simple language and convey some of the problems involved. So there's undoubtedly a demand for knowledge from the general public but it needs to be well informed. It can only come from the experts.

REFERENCES

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