threatened abortion. Herbst's finding seems to have been the first clinical evidence that foetal exposure to a carcinogen can cause cancer, and it also bridged the gap between animal feeding studies and direct observation in man (Herbst, A. L., Ulfelder, H., and Poskanzer, D. C., *New England J. Med,* **284**, 878; 1971).

Although the two findings are essentially irrelevant to the purposes of the Delaney Amendment, which requires only that DES causes cancer in animals for it to be banned from the food supply, they have cast doubts on the FDA's testing procedure and raised the spectre of risks from amounts of DES in meat and liver which may be below the detection threshold.

The issue is complicated by the fact that DES is no different from other natural and synthetic hormones in its carcinogenicity, and that the small amounts that may be present in meat are negligible compared with the quantities to which people are naturally exposed from their own glands and even plants. At earlier hearings before Mr Fountain's committee, it was suggested that 500 pounds of liver contaminated with DES at the level of 2 parts per thousand million would contain the same amount of oestrogen as that produced by a premenopausal woman in a day.

Others argue, however, that DES is several times more powerful as an oestrogen than oestradiol, the natural hormone, and that it is several thousand times more potent than the most potent plant hormone. A direct comparison between the amount likely to be ingested in meat and the daily production in man is therefore misleading. And where carcinogens are concerned, is not the only safe level none at all? Dr Umberto Saffiotti, Associate Scientific Director for Carcinogenesis at the National Cancer Institute, suggested at Mr Fountain's hearings that there is a strong case for not allowing any chemical carcinogens in food use. "I think it is a very prudent policy which is being widely accepted by people in cancer research."

DRUG ABUSE

Antagonists in Sight

by our Washington Correspondent

It is now nearly five months since Congress passed legislation formally establishing the Special Action Office for Drug Abuse Prevention in the White House, and the office has already made its presence felt in several ways. Its first action was to urge on the recent decision to make methadone more widely available for treating heroin addicts (see *Nature,* **236**, 322; 1972). Now, Dr Jerome Jaffe, Director of the Special Action Office, has announced that the National Institute of Mental Health is to expand research on narcotic antagonists.

Both policies are logical in the light of Dr Jaffe's own professional background. Jaffe pioneered methadone maintenance in Illinois before joining the Administration and was also responsible for much of the early work on cyclazocine, the most widely studied narcotic antagonist. But the two moves also fit in with past policies for combating the rising tide of drug addiction in the United States—because of the size of the problem and the political and social need to find a quick solution, much effort has been expended on trying to find a technological fix in the shape of drugs which will help an addict to break his habit or even help to avoid addiction. One noticeable benefit has been a loosening of the pursestrings for pharmacological research.

Several directions of research are being opened up. They include attempts to develop a non-addictive analgesic for medical practice, efforts to find long-lasting potent drugs to block the euphoric effects of heroin without causing side effects and—a long shot—an attempt to demonstrate antibodies to heroin which might be used in vaccinations to prevent addiction. Tying these projects together is an extensive body of basic research on the underlying biochemical basis of addiction. Until there is a well established model for addiction at the molecular level, the search for a technological fix will at best be hit and miss.

How is the programme going? It is only fair to say that everybody concerned with drug addiction accepts that drugs by themselves cannot provide the whole of a solution to drug abuse, for psychological factors lead to addiction in the first place. But those who would use drugs to treat addiction argue that drugs have a useful part to play alongside other approaches such as group therapy and psychological counselling, and that they can in some cases be stepping stones to a cure. William E. Bunney, jun., Director of the NIMH Division of Narcotic Addiction and Drug Abuse, said last week that "we are at a point where there is cause for optimism that we can develop effective antagonistic drugs".

This remark came with the announcement that grants totalling more than $2 million are to be awarded for clinical and pre-clinical testing of narcotic antagonists, and to support a conference on the topic later this year. The clinical research will be chiefly confined to cyclazocine, used on heroin addicts in various stages of withdrawal and in a variety of psychological surroundings. The clinical research will be focused on other possible narcotic antagonists which have shown promise in animal studies. The new programme also represents a considerable expansion of present basic pre-clinical research on narcotic antagonists, now running at about $1 million a year.

Antagonists function by sitting on receptor sites in the brain, thereby preventing access to the receptors of opiate molecules. The antagonist will also displace opiate from the receptor, so that if it is administered after an opiate, it will quickly nullify the effects of the drug and produce withdrawal symptoms in an addicted person. If it is given before an opiate, on the other hand, it will prevent effects.

Antagonists have two potential uses. First, administration of an antagonist may help an addict who has recently been withdrawn from heroin to stay drug-free by blocking euphoric effects and thus removing the reinforcement of drug-seeking behaviour. The most promising application of antagonists may be their use to prevent people who have been experimenting with heroin from becoming addicts. Dr Jaffe suggested last week that since rapid and reliable tests to detect heroin use are now available, "some medical or community groups may elect to use such techniques in high risk populations . . . and thereby discover heroin experimenters before they become addicted, involved in crime, or die of overdoses. Once diagnosed, these early potential addicts could be temporarily immunized by daily treatment with antagonists."

The snag is that no available antagonist is ideal for widespread use. To be offered in a drug treatment programme, antagonists would have to be orally administered, potent, have few side effects and produce no tolerance. But cyclazocine, the most widely studied drug, produces headaches, blurred vision, sedation, feelings of depersonalization, and hallucinations. Patients can, however, become tolerant to the side effects if the drug is administered over several days. Another widely studied antagonist, naloxone, produces very few side effects, but its antagonistic effects last for only four to six hours, compared with 24 hours for cyclazocine. But animal studies on a drug with the code name EN–1639 A suggest that it may be three times more potent than cyclazocine, last for a day and produce few side effects. It has not yet been given clinical trials, however.

Whether or not clinical trials with the new antagonists turn up an effective agent, it is clear that the most important task for improving rehabilitation and treatment for heroin addicts is to expand and improve drug addiction clinics. There are signs that Jaffe's office is conscious of the need, and facilities are indeed slowly being improved, but there is clearly need for expansion. The opening of a new clinic is, however, not such a newsworthy event as progress towards the technological fix.