mechanical factors were dominant, the symmetry of the disease in many of the patients was perhaps more striking than the difference between right and left. Nevertheless, the more active limbs did seem to develop the more severe arthritic changes, and the wrist involvement did appear to begin at an earlier stage. Asymmetry was noted to be more common in seronegative cases. In the present series both seronegative and seropositive cases showed asymmetry.

The experiments of Courtwright and Kuzell (1965) are very pertinent. In 20 out of 31 rats with adjuvant polyarthritis, prior section of one sciatic nerve appeared to delay the onset and diminish the severity of the arthritis in the operated limb. Similar but less marked sparing of joints resulted from prior fracturing of the femur. These two workers attributed their results to an interruption of the normal neurological control of the limb concerned rather than to mechanical factors, but the findings of this series, and their results, also correlate with different experimental work.

Dumonde and Glynn (1962), after rendering rabbits hypersensitive to their own fibrin, were able to produce an arthritis with histology similar to rheumatoid arthritis by intra-articular injection of fibrin.

Norton and Ziff (1966) injected colloidal gold particles into a joint. At synovectomy, about an hour later, these were found deep in the synovial membrane. They consider that the joint space is in continuity with the synovial extracellular space and regard the gold particles as having been mechanically propelled into their deep situation.

If, therefore, fibrin or some other immunizing agent—perhaps a globulin complex present in the joint space—is forced into the synovium by exercise or joint movements, it might be expected that in rheumatoid arthritis joint usage would increase the severity of the disease and paralysis would minimize the inflammatory process.

The actual mechanical factor involved may be the intra-articular pressure. Dixon and Grant (1964) have shown the high pressure reached when a joint is used actively, and though this work has not been repeated on joints of paralysed limbs it is reasonable to assume that, whatever stresses occur in such joints, the intra-articular pressure does not reach the levels produced in normal limbs. It is conceivable that capsular and ligamentous stresses might even be higher in a paralysed weight-bearing limb.

Glyn *et al.* (1966) have studied the incidence of osteoarthritis in people with limb paralysis occurring after poliomyelitis. They found a positive correlation between the severity of degenerative joint changes and the power of the muscles controlling the joint. The flail limbs were relatively free from arthritis. However, it is not clear how much can be inferred between the two different types of arthritis.

What does seem clear is that after muscle paralysis the associated joints show less destructive changes of both degenerative and inflammatory arthritis than joints in the non-paralysed limbs.

The problem arises of how far these findings should influence decisions regarding rest and exercise in the management of arthritis.

Summary

Details are given of 12 cases of rheumatoid arthritis occurring in people previously paralysed by poliomyelitis. Joints controlled by the paralysed muscles were less affected than those in the contralateral non-paralysed limb. This sparing effect was most marked in completely flail limbs.

Subcutaneous nodules showed similar asymmetrical distribution in two patients.

It is suggested that decreased intra-articular pressure might be an important factor in this apparently mechanical effect.

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Adverse Reactions from the Illicit Use of Lysergide

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Lysergide (lysergic acid diethylamide ; L.S.D.) is a drug with marked effects on the mind. Illegal use of the drug in the United States has led to reports of untoward and adverse reactions (Cohen and Ditman, 1962, 1963 ; Ludwig and Levine, 1965 ; Frosch *et al.*, 1965). Severe abnormal reactions have also occurred in the United Kingdom when the drug has been obtained illicitly and taken without medical supervision, and some are reported here.

Case 1

A youth aged 19 was educated at a grammar school but failed G.C.E., and after leaving school at the age of 16 never worked. He then lived a vagrant existence and at different times took marijuana, oral amphetamines, intravenous heroin and cocaine, and methylamphetamine hydrochloride (Methedrine) intramuscularly. He had always obtained drugs illegally. When he first took L.S.D. he had a short-lived paranoid psychotic reaction.

"I had a bad trip the first time I took it. I thought I was in a different place to where I was. I was very frightened ; I thought people were coming after me. All these red people were coming after me for some reason. I was very scared and ran out of the room. I thought they would get me. I did not know if they were the devil's people or something. I was running about the streets scared. I don't know what happened for about four hours ; I was very frightened and running about the streets."

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Despite the unpleasantness of this first experience he continued to experiment with L.S.D., but did not have a similar reaction on subsequent occasions. "I never had a bad trip since then. I use it to expand my mind. I'm not against it now. I get a really wonderful experience. I use it for relaxation with music. I underestimated it the first time I took it. It took me unawares."

His current problem is physical dependence on heroin.

Case 2

A man aged 24 had a normal upbringing and education at a secondary modern school until he was 15. Then he had periods in an approved school, Borstal, and two years' imprisonment for receiving. He had taken dexamphetamine since the age of 16 and also marijuana, heroin, and cocaine. He had a cocaine psychosis with hallucinations on one occasion. He took L.S.D. once and found that he became acutely depressed and suicidal. "I felt like jumping into a pond. I had a crazy urge to." He found the experience sufficiently frightening and unpleasant to have no desire to repeat it. He had a history of depressive reactions and he slashed his wrists on one occasion in hospital, after attending the funeral of his best friend, who had committed suicide.

Case 3

A man aged 21 had a normal childhood and had done well at grammar school until he was 17, when he left after taking O levels. He then did hotel and catering training for two years and obtained a job as assistant manager of an off-licence. He was described as quiet and studious up to the age of 19. He had his own car and saved money. He started taking amphetamines at 18, and this was succeeded by experimentation with all forms of drugs. He took heroin, cannabis, and "sleeping tablets" irregularly. He tried L.S.D. once and found the effects pleasant at the time. "At first it was a vague dream. I was semi-floating. There's nothing you can't do. You throw your problems aside, think you are God." However, he had severe panic attacks later. "The after-effects were too terrifying. I would not want to repeat it. I was violently sick for a few days, my head was spinning, and I could hardly stand. I was in a deep depression and thought someone was watching me all the time. I would wake in a cold sweat, find myself lying in bed paralysed. Once you move your arm you are all right, you sit up after 20 minutes. It's frightening, you wake up and don't know if you are awake or not." He had no desire to take L.S.D. again. He had become heavily dependent on alcohol and was drinking a bottle of brandy a day, mixing it with Pernod. He had been incapable of working for two months and had spent all his savings and sold his car.

Case 4

A man aged 21 had had a very disturbed childhood and upbringing. His parents were divorced and remarried, and he was brought up by various relatives and in foster-homes. He had nocturnal enuresis until the age of 15. He was in the Merchant Navy for three years (aged 16–19). After this he had not worked. He lived with a prostitute, sold hashish, and touted for blue films in the West End of London. He was currently on probation for living on immoral earnings. He attended a V.D. clinic regularly, having had gonorrhoea several times according to his own account. He had taken amphetamines and marijuana since the age of 18, and had once jumped in front of a taxi while under the influence of amphetamines. He started taking L.S.D. and took it three times in a week. He found it produced pleasant reactions at first but later unpleasant ones, and he stopped taking it.

"It was great when it first happened, but after a while I began to get the horrors. It frightened me and I started to fight under it. Once when on L.S.D. I used violence. Two of us had taken L.S.D., me and this girl. There were two other couples, one couple I knew well, the other I did not. I thought this bloke was trying to get off with this girl I was taking a trip with. We were talking, laughing, drinking. In the hall there were me and this girl and the other fellow. He said, 'Go away please.' I went mad and started to fight him, but I cooled down quickly. I said, 'Go away for a minute.' I was frightened of him, so afterwards I apologized. I did not know how to apologize enough."

After this he stopped taking L.S.D., but continued to smoke marijuana. He found that although he had never had any unpleasant effects from smoking cannabis before he used L.S.D., when he smoked it again, after his experimentation, he began to get recurrent short-lived psychoses. "I used to smoke hashish till I could not think. I'd smoke myself silly with some friends. If I smoked with them I'd smoke an awful lot. Now, more recently, I've realized it was since taking L.S.D. I was getting more horrors. I keep getting double meanings. I was really terrified the night before last, I was just smoking hash at the time, I could see the effects like L.S.D. I thought they were wanting to kill me. I was sitting looking at myself in a mirror. They were talking about vans. I thought it was all directed at me, it was driving me nuts. I thought people were going to kill me. It was worse than after I had the L.S.D."

He found these reactions sufficiently alarming to wish to try to give up all use of drugs.

Case 5

A man aged 20 died from severe laceration of the brain associated with a fracture of the left parietal region caused by falling from a fourth-storey window on to a brick wall. This appeared to have followed his first experimentation with L.S.D.

He was a musician living in furnished rooms and had no past history of mental illness or instability. He had previously smoked marijuana and belonged to a group of people who used drugs and were interested in them. He was anxious to try the effects of L.S.D., and arranged to do this with two friends, one of whom had taken the drug before and who possessed some. On the day that this was arranged both these friends apparently changed their minds and did not go round to his room. That evening he was seen to climb out of the window of his attic room, having first broken the glass; he stumbled, slid down the roof, and fell to his death. The door of his room was found to be locked and barricaded on the inside with a chair against the door. The room was in complete disorder, with clothing, bedding, and furniture strewn all over the room. No one else was present. The gas-stove and the electric-light fittings were broken. All the windows in the room were broken, including the one he had got out of.

At necropsy it was not possible to confirm the presence of L.S.D., though it appears likely that it had been taken. There was no evidence at necropsy that he had taken any other drugs, such as amphetamines.

Case 6

A man aged 20 died from multiple injuries (fractured skull, fractured pelvis, fractured right tibia and fibula) caused by jumping or falling 60–70 ft. (18–21 m.) from a church roof. He was a bricklayer's labourer and had no history of serious illness or accident, nor was there any history that he had previously taken L.S.D. On the Saturday night before his death he apparently went to a club in Soho with a girl, who could not subsequently be traced. On Sunday morning at 10 o'clock he was found lying naked in the forecourt of a church in Highgate. His clothes had been left in a neat pile on the roof. Necropsy showed that he had died from multiple severe injuries, and analysis of specimens of blood (peripheral), liver blood, heart blood, bile, and stomach contents gave the following results (Dr. Ann E. Robinson): "(1) Routine screening tests for alcohol and 5,5-disubstituted barbituric acid derivatives in the peripheral blood sample were negative. The stomach contents also gave negative results from these substances. (2) The specimens of bile (6 ml.) and the remaining peripheral blood (11 ml.) were examined for the presence of lysergic acid diethylamide (L.S.D. 25). A substance was detected in both of these samples which had properties consistent with those of L.S.D. 25, though unequivocal proof of identity of the recovered substance was lacking."

It seems likely that this man had taken L.S.D. at some stage after his visit to the club and had then climbed to the top of a church, taken all his clothes off, put them in a neat pile, and jumped or fell to his death. It is possible that he had a psychotic reaction or he may have had such changes in mood (euphoria or elation) that he believed he could float safely down.

Discussion

There has been an increase recently in the use of L.S.D. in this country on a casual basis and not under medical supervision. Use in this way as a "mind-expanding" drug has been extensively discussed in the press and on television, and has been advocated in non-medical journals. After a similar interest in the non-medical uses of the drug and extensive self-medication by fringe groups in New York there was a sudden upsurge of admissions to Bellevue Hospital with acute reactions from its use (Frosch *et al.*, 1965). These fell into three groups: (1) acute panic reactions; (2) recurrence of symptoms while abstaining from the drug, which was more likely to occur after multiple ingestion; and (3) prolonged psychosis.

Cases 1, 2, and 5 reported here appeared to be acute panic reactions, and Cases 3 and 4 a recurrence of symptoms in a period of abstinence. Case 4 also showed signs of a prolonged psychosis. Case 6 may have been due to disordered judgement or a psychotic reaction. Prolonged adverse reactions, including chronic hallucinatory states, also occur (Rosenthal, 1964). Owing to the fashion of using sugar cubes as a vehicle for black market L.S.D. it can also be taken accidentally—for example, by children—and three such cases have been reported. One of these sustained a dissociative state, accompanied by anxiety and visual illusions, that lasted for several weeks (Cohen, 1966). Cases 5 and 6 show the need to look for L.S.D. and amphetamines at necropsy in deaths of this type, lest some be wrongly attributed to suicide.

Despite the statements of the protagonists of the use of this drug that it is safe, L.S.D. can be dangerous when taken casually—for example, when not taken by selected patients under strict medical supervision and with the use of proper safeguards. The incidence of adverse effects associated with controlled use of the drug by physicians suggested that in medical hands it was an exceptionally safe drug (Levine and Ludwig, 1964).

Summary

Recently there has been an increase in the use of lysergide (lysergic acid diethylamide; L.S.D.) obtained illicitly. Adverse reactions are not uncommon, and six (two fatal) cases are reported.

I am grateful to Professor F. E. Camps, Dr. A. Robinson, and Mr. F. F. Haddock for help with information about some of these cases.

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Preliminary Communications

Trephine Biopsy for Diffuse Lung Lesions

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Drill biopsy of various tissues by means of a dental drill and cylindrical rotating cutting needle was described by Kirschner (1935). The technique was modified by Christiansen (1940) and further results with this method were reported by Ellis (1947). A high-speed pneumatic drill was used by Deeley (1960). Within the thorax, these authors confined themselves to the diagnosis of peripheral tumours adherent or adjacent to the chest wall, and, despite the theoretical advantages of the procedure over other methods of lung biopsy, interest in it has lapsed because of this limited application. It is our purpose to show how high-speed drill biopsy can be extended to the diagnosis of diffuse pulmonary conditions.

The extremely fast cutting edge provided by the air-drill was found to be effective in obtaining specimens from the lung at necropsy, but the small trephine described by Deeley failed to provide adequate specimens of diffuse lesions from inflated lung. To overcome this difficulty a large trephine with special features was designed by one of us (S. J. S.) and proved successful experimentally and in practice.

Indications

Indications include diffuse and localized lesions of the lung or pleura where a definitive diagnosis is required for the purpose of treatment, prognosis, or a claim for industrial compensation.

There are no specific contraindications other than bullae, cysts, or aneurysms, but it is wise to avoid patients with a bleeding diathesis or insufficient respiratory reserve to risk a pneumothorax. Some upper-lobe lesions may prove inaccessible and those adjacent to the mediastinum are best avoided.

Method

The apparatus consists of a small Desoutter pneumatic drill easily held in the hand and driven by compressed air from a cylinder fitted with a reducing valve. A speed of up to 15,000 revolutions per minute at a pressure of 100 lb./sq. in. (7 kg./sq. cm.) is controlled by a trigger. The spindle of the drill is connected by a Luer fitting to a hollow trephine 7.5 cm. long and 3 mm. in external and 2.1 mm. in internal diameter, with a right-angled smooth cutting edge. The trephine is rifled internally for 5 mm. behind the cutting edge to guide the specimen into its lumen, and fitted with a sharp-pointed keyed stylet projecting 2.5 mm. beyond the end (Fig. 1).

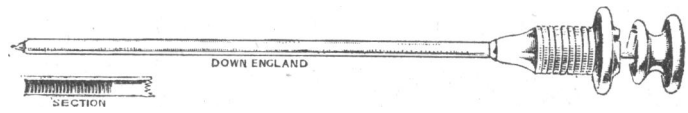

FIG. 1.—Lung biopsy trephine for use with high-speed air-drill. Length 7.5 cm., external diameter 3 mm., internal diameter 2.1 mm. Internal rifling for 5 mm. at end. Sharp-pointed keyed stylet fitted.

The first step is to choose a suitable site with chest radiographs and markers. If the lesion is diffuse and bilateral the most convenient position is usually the eighth right intercostal space posteriorly with the patient sitting across the bed and leaning forward, but an axillary or anterior approach may be used with the patient lying down. Premedication is not usually necessary, but it is essential to demonstrate the apparatus to familiarize the patient with the whistling noise produced by