This strain has two populations of *Staph. aureus*, one of which shows standard sensitivity to methicillin while the other, minority, population of cells shows resistance to 25 µg./ml. Through the kindness of Dr. Jevons I had an early opportunity of examining this strain, with results in no way different from her own or those of Rolinson and Knox. The minority population of resistant cells has colonial and other properties different from those of typical *Staph. aureus*, but, in so far as it was isolated from two individuals, neither of whom had received methicillin, in an environment in which the drug was not being used, it must clearly be accepted as the first naturally resistant strain. Since then I have learned of one other similar strain (Elek, 1961, personal communication). It is clear, therefore, that natural resistance can occur, but the data at present available suggest that this is of a very low order of frequency—on Jevons's figures alone, one out of 5,440 strains examined. This is probably much lower than the original frequency of natural resistance to penicillin G, but time alone will tell whether or not such strains are the progenitors of an increasing resistant population.

The results reported here also reveal further differences between the action of methicillin and penicillin G, as well as between *Staph. albus* and *Staph. aureus*. With the reservation quoted above, there is ample evidence that all typical strains of *Staph. aureus* are fully sensitive to methicillin, irrespectively of any resistance which they might possess to penicillin G (Thompson *et al.*, 1960; Rolinson *et al.*, 1960; Stewart, 1960a; Garrod, 1960; Jevons, 1961). The strains of *Staph. albus* described here with resistance to methicillin, show cross-resistance to penicillin G. Resistance of *Staph. aureus* to penicillin G is often associated with penicillinase-production, but the resistant strains of *Staph. albus* studied here produce no substances capable of completely inactivating methicillin. The resistant mutants of *Staph. aureus* described by Barber (1960) equally failed to inactivate methicillin. It is clear, therefore, that the mechanisms associated with staphylococcal resistance to the natural benzylpenicillins do not account for acquisition of resistance to the synthetic derivative methicillin.

Largely as a result of studies *in vitro*, there has been a tendency recently (*British Medical Journal*, 1961) to regard methicillin as a drug which should be kept in reserve for difficult staphylococcal infections lest more widespread use should lead to acquisition of resistance on the part of the organisms. The present studies do not support this view: naturally resistant strains of *Staph. aureus* are very rare indeed; resistance develops with difficulty *in vitro*, and, on present evidence, not at all *in vivo*; and the drug is not destroyed by penicillinase-forming staphylococci. If these properties are considered in relation to its powerful bactericidal action, lack of toxicity, and undoubted therapeutic effect even in severe infections (Douthwaite and Trafford, 1960; Stewart *et al.*, 1960), methicillin would appear to be the most effective antistaphylococcal agent available. Its disadvantages—narrow spectrum and parenteral administration—might even serve a purpose by restricting its use to precisely those infections—that is, those due to *Staph. aureus*—for which it is specifically indicated and in which it has a unique life-saving effect.

Summary

Freshly isolated strains of staphylococci were investigated for evidence of resistance to methicillin.

Some strains of *Staphylococcus aureus* showed a limited capacity to develop resistance artificially *in vitro*; there was no evidence of resistance *in vivo* in strains reisolated from patients and carriers treated with methicillin, even under conditions favouring the emergence of resistant strains.

Staph. albus acquired a high degree of drug-resistance readily *in vitro*; a lesser degree of resistance developed in strains reisolated from patients during prolonged therapy with methicillin.

Resistant strains of *Staph. albus* showed cross-resistance to penicillin G but did not form penicillinase.

Resistance to this form of synthetic penicillin appeared to depend on mechanisms different from those involved in resistance to penicillin G.

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ELECTROENCEPHALOGRAPHIC CHANGES IN CEYLONESE BOXERS

BY

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The recent publications in the local press and the articles in foreign periodicals about the fatalities and hazards of boxing prompted us to carry out a study of the electroencephalographic changes (if any) in Ceylonese boxers. We were especially interested in this study, as we noticed that some of our university boxers showed definite changes in their attitude to work and also significant E.E.G. changes when we were carrying out our routine medical tests.

Several workers have described the changes that could take place during either amateur or professional boxing. Busse and Silverman (1952), studying the E.E.G. changes in 24 professional boxers, found dysrhythmic E.E.G.s in 37.5% of these boxers. There was some evidence that men who had been knocked out showed severer E.E.G. disturbances than those who had

not been knocked out. They also noticed that focal disturbances were more frequent in the younger men than in the older men, and the latter group, generally speaking, had fewer E.E.G. disturbances. Larsson *et al.* (1954), in their study of the clinical and E.E.G. changes in boxers, found that 52% of their cases showed a pathological E.E.G. after the matches. Milroy Paul (1957) described a case of traumatic decerebrate rigidity in a Ceylonese boxer who died as a result of a blow on the chin. Macdonald Critchley (1957) described in detail the medical aspects of boxing from a neurological point of view. According to him there are non-specific E.E.G. changes in some boxers; he also states that most of the available evidence on the E.E.G.s of boxers is rather contradictory.

Several discussions and letters on boxing have appeared in the *British Medical Journal*, and recently a motion was brought forward at the Annual Meeting of the British Medical Association calling on the Government to declare boxing illegal (*British Medical Journal*, 1960).

Material and Method

A total of 50 Ceylonese boxers were examined by us; they were drawn from the Ceylon University, Police, Army, Navy, R.Cy.A.F., and some of the secondary schools. In this group were included the best boxers of the island, who have even represented Ceylon at meetings held abroad. They had been in training for periods varying from 1 year to 18 years, and appeared to be clinically "normal" and to be able to carry out their normal duties. As a control group we had 75 (55 males, 20 females) Ceylonese adults drawn from the Ceylon University who were not boxers. Our investigations in both groups consisted in taking a complete case history, and this was followed by an E.E.G. examination under identical conditions for each case. For the E.E.G. examination the subject was made to rest on a couch and relax with the eyes closed. The records were taken on an eight-channel Grass E.E.G. machine using needle electrodes, and both scalp-to-ear and scalp-to-scalp techniques were used in all cases. Recordings were made from the frontal, parietal, occipital, and temporal areas. In most cases we tried to induce activity by using a Grass photic stimulator and also by hyperventilation.

Analysis of the records were made by studying the amplitude and frequency of the recordings and looking for the presence of large slow waves or the appearance of high-amplitude spike potentials in the different leads. No case was considered abnormal unless the large slow waves or spontaneous spikes appeared repeatedly in both the "unipolar" and bipolar recordings. Further, it was generally noticed that these abnormal changes were thrown out by either photic stimulation or hyperventilation.

Results in Control Group

In our control group of 75 University students we had a sample of young men and women who took part in other sports but not in boxing. An analysis of their E.E.G. records (at rest) shows that six cases (8%) revealed spontaneous bursts of abnormal activity—that is, either high-amplitude spikes or large slow waves of 4–7 c.p.s.). The rest of the control tracings were within the limits of normal variation and consisted of 8–12 c.p.s. activity with an amplitude of 30–50 microvolts.

Results in Boxers

The boxers were examined and a careful history was first taken to eliminate, so far as possible, head injuries from any other cause. There were four rugger players and two wrestlers amongst our group, and only one rugger player gave a definite history of being knocked out twice during games. While recording their histories we questioned them especially for (a) any knock-outs during their boxing career, (b) frequent attacks of headaches, and (c) loss or impairment of memory.

Seventeen (34%) gave a history of at least one knock-out, while six (12%) complained of persistent headaches, and 11 (22%) of loss or impairment of memory. It was interesting to note that some boxers actually said, "Doctor, I regret having taken up boxing; I will never allow my sons to box."

A careful analysis of the E.E.G. recordings of these 50 boxers showed that 30 (60%) showed spontaneous bursts of disordered activity. The criteria we used to classify a record as abnormal have already been mentioned.

Below are three cases of which we give a brief history and the E.E.G. findings.

Case 1.—This man, aged 25, had boxed since 1948. He represented Ceylon in the 1952 Asian Games, the 1956 Olympics in Melbourne, the 1957 S.E.A. Championship meeting in Burma, the 1958 Empire Games in Cardiff, and the 1959 Indo-Ceylon meeting in India. He gave no history of knock-outs but complained of impairment of memory.

FIG. 1.—Case 1. Spontaneous bursts of disordered activity occurring in several leads.

FIG. 2.—Case 2. Spontaneous bursts of spikes and slow waves occurring in several areas simultaneously.

He has felt "dazed" after hard blows on the head. E.E.G. recordings taken at rest showed sporadic bursts of disordered activity in both "unipolar" and bipolar records (Fig. 1).

Case 2.—This man, aged 27, had boxed for the last five years. He did not complain of headaches or loss of memory, but had had one knock-out and was unconscious for eight hours (two years before the E.E.G. recording was made). His E.E.G. showed spontaneous bursts of disordered activity (Fig. 2).

Case 3.—This man, aged 21, had boxed from 1952 to 1956; he then stopped until 1960. He gave a history of having been struck by a stone on the head in 1954 and was unconscious for about two hours on that occasion. He complained of frequent attacks of headaches and was referred to us for an E.E.G. in May, 1960. The E.E.G. was reported as being within the limits of normal variation (Fig. 3). In August, 1960, he was sent for an E.E.G. as he was unconscious for about 20 minutes after a blow on the chin during a university boxing meet. This E.E.G. was taken three days after the "knock-out." The recording showed spontaneous bursts of disordered activity (Fig. 4).

FIG. 3.—Case 3. No abnormal E.E.G. changes before the knock-out. (Record taken in May, 1960.)

FIG. 4.—Case 3. Spontaneous bursts of disordered activity occurring in several leads. (Record taken in August, 1960.)

Discussion

The variations found in our control group of cases (8%) is well within the expected figures. The presence of disordered activity among 60% of the boxers is statistically very significant. Further, it is noticed that, although only 34% of the boxers gave a history of knock-outs, 60% showed disordered activity. Our findings therefore show that E.E.G. recordings of boxers taken under identical conditions (at rest) show a significant change in the wave form in a large percentage of cases.

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BLOOD-GROUP STUDIES IN FRIEDREICH'S ATAXIA

BY

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Few inherited characteristics can be followed accurately from one generation to another. Those that can be traced include sex, an ability to taste phenylthiocarbamide (P.T.C.), and the blood groups. While linkage of disease with sex has been known for a very long time, linkage of the blood groups ABO and rhesus with the hereditary conditions of the nail-patellar syndrome and oval red cells respectively has been discovered more recently (Renwick and Lawler, 1955; Goodall *et al.*, 1953). As the number of blood groups which have been discovered increases, the chances of detecting linkage become more probable, linkage being easiest to demonstrate in those groups whose alleles are fairly evenly demonstrated in the population, such as the Lewis factor (Race and Sanger, 1958).

In the hereditary ataxias, Hogben and Pollack (1935), Haldane (1941), and Schut (1951) have carried out linkage studies. Hogben and Pollack deal with 22 families affected by recessive Friedreich's ataxia; and by a production method devised by Hogben they found no reason to suppose that this type of Friedreich's ataxia could be linked with the inheritance of the ABO group or the ability to taste P.T.C. In Haldane's cases transmission in some cases was believed by him to be partially sex-linked, and in others it was dominant; in neither type was there any apparent linkage with ABO blood group or P.T.C. appreciation. Schut, who included in his paper the result of tests involving ABO, rhesus, MN, and Kell blood groups, the tasting of P.T.C., and the sex distribution, was investigating a family in which hereditary ataxia occurred in six generations. He could find no evidence to suggest linkage with these characteristics. Here transmission was by dominant genes, and not all the affected persons exhibited pure Friedreich's ataxia. There is little to suggest that recessive and dominant Friedreich's ataxia have anything in common genetically, although the neurological picture may vary only in age of onset.

The Investigation

The present study has been carried out on the members of the eight families described elsewhere (Powell and Childers, 1961), in all of which transmission was by recessive genes. Linkage has been sought between this condition and nine blood groups (see Table). The study includes all the surviving parents (11 out of 16), 17 of the affected members, and those healthy members who have not emigrated (14 out of a possible 31).