essentially "fingerprints" fragments of DNA. By now the Cambridge group has 860 such fragments, but, says Brenner, "these are islands, and we have to fill in the gaps."

The clearly stated limitations of mapping techniques so far available led to a recognition that a map, however good, might remain patchy for a long time. "The endgame is indeterminate," said Brenner, "and it shouldn't be counted in estimates of the cost of the project." The discussions also led to the notion of combining cosmid mapping with a restriction fragment length polymorphism (rflp) map, the latter forming a very much coarser scatter of markers that would serve to pinpoint the position of cosmids around the genome.

The development of new techniques both for mapping and sequencing is going to be crucial to bringing the genome project within manageable bounds, and Academy committee members were therefore delighted to hear from Harvard University's George Church about "multiplex sequencing." If it works, this low technology, parallel processing approach has the potential to improve sequencing by a factor of 10. Church and his colleagues are now putting the system to the test, and if it is successful they hope to have sequenced 90% of the *Escherichia coli* genome [which has 3 megabases] within a year.

The very real momentum that is now established behind the genome project nevertheless faces many uncertainties. For instance, proponents' interest in establishing a series of small, specialized centers reflects a recognition of the need for some sort of coordination and organization while maintaining flexibility, specifically in technology development. Although the prospect of trudging through the entire genome, whether mapping or sequencing, is widely described as being potentially immensely tedious, there is a fear that if a megacenter is established too soon to take on the job as a production task, then the technology might become frozen in its infancy. "A factory is not the place you solve problems," observed one committee member.

Together with questions of organization inevitably come questions of funding. The figure of $3 billion is rarely heard these days. Instead, estimates of something between $30 million and $50 million a year for 10 years are much more common, which brings the project well within a scale of annual expenditure that, for instance, the DOE could cope with if it so chose. The maneuvering is just beginning over which agency will eventually take charge of the principal responsibility for the human genome project. ■ ROGER LEWIN

Debate over Emergence of Human Tooth Pattern

For more than a decade, anthropologists have accepted that early human ancestors had a prolonged infancy period, like modern humans; this idea is now being challenged

"THE question of standards might sound like a mild issue," says Holly Smith of the University of Michigan, "but it is really a massive disagreement." Smith is referring to the guts of a dispute that is fomenting between herself and Alan Mann of the University of Pennsylvania. The dispute centers on how you interpret the patterns of dental growth and development in our 2-million-year-old ancestors: are the patterns like those of modern humans or more like those of apes?

The disagreement, which so far has reached the scientific literature only in simple declarative form, extends beyond Smith and Mann and includes Timothy Bromage and Christopher Dean, two researchers at University College, London. Bromage and Dean believe, like Smith, that the teeth of the early hominids were distinctly primitive and apelike in their overall growth characteristics. Mann vigorously rejects the notion and insists that by at least 2 million years ago our ancestors had already evolved a pattern of dental development that is seen in modern man, *Homo sapiens*.

Smith and Bromage and Dean independently published their conclusions relatively recently, thereby challenging the conventional wisdom established by Mann more than a decade ago. Mann has been criticizing these conclusions during the past few months in several small seminars and now has two stinging critiques prepared for publication in the scientific literature. "Their analyses," he says, "are absolutely and completely wrong."

The distinction between the two patterns of dental growth is significant in this context because, as Washington University anthropologist Glenn Conroy says, "it affects the way you think about these creatures." The reason is that, by comparison with apes, modern humans have an extended period of infancy, which is important for the greater intellectual and social nurturing to which we must be exposed. If our earliest ancestors also had prolonged infancies, then it is perhaps legitimate to infer that they had already begun to assume a degree of humanness that is not shared by "mere" apes. Signs of prolonged infancy are directly reflected in the growth characteristics of the dentition: hence the interest in the teeth of the early hominids.

The suggestion by Smith, Bromage, and Dean that hominids of 2 million or so years ago were in general more apelike than humanlike falls very much in line with current thinking about human evolution. For instance, most anthropologists now agree that the evidence of molecular biology demonstrates a much closer genetic relationship and more recent common ancestry with the African great apes than had previously been contemplated. And there is a lot of talk nowadays about how some of the earliest hominids spent a good deal of time climbing trees, which has a distinct simian ring to it.

Overall, then, there has been a distinct shift during recent years from thinking about our earliest relatives as being quaint and hairy diminutive humans to characterizing them as bipedal apes. The question here, then, is how real is this trend? "I would term it a fashion," says Mann, who characterizes himself as one of the last old-time anthropologists.

The story began in the late 1960s with Mann's pioneering work applying x-ray analysis to the fossil remains of the cave site of Swartkrans in South Africa. Mann chose this site because it contained the largest collection of early hominid juvenile jaws available anywhere in the continent. The work has to be done on juvenile jaws, because you need to be able to see tooth patterns while development is still incomplete. Mann's conclusion, which he extended by further work in the early 1970s, was that the Swartkrans hominids had dental growth characteristics—and therefore duration of infancy—very like modern humans.

"I was concerned with looking for shifts," recalls Mann. "I felt that only minor genetic changes would be required to elongate the postnatal developmental stages. This would have an important effect on allowing animals to internalize a lot more information about their environment." Mann's conclusions were in harmony with ideas about hominid brain development that were then current, and the publication of his 1975 monograph on dental patterns established conventional thinking for a decade.

For any fossil jaw to be accepted as hominid it therefore had to display the humanlike pattern of dental development. The dogma was so strong that it sometimes seduced people into seeing a humanlike pattern where in fact no such pattern existed. One classic example was with a 15-million-year-old ape, *Ramapithecus*, which during the 1960s and '70s was considered by many to be the earliest of all the hominids. When its tooth pattern was examined, it was declared to be human. Later, claims for the hominid status of *Ramapithecus* were abandoned, as were ideas about its putative human dental pattern.

Although the late George Sacher, a zoologist, suggested in the mid-1970s that, because of their small body size and brain size, the early hominids were unlikely to have had a prolonged period of infancy, the first serious and successful challenge to Mann's ideas came in 1985 from Bromage and Dean. What began as a study of the growth patterns of the face and cranium of early hominids produced as an unexpected bonus some surprising information on the rate of growth of their teeth. The implication was that the period of infancy in early hominids was not significantly prolonged at all, and was much more in line with apes.

Bromage announced this proposal at the 60th anniversary meeting of the discovery in South Africa of the first early hominid, known as the Taung child. He said that Taung, which had been judged on human dental criteria to be about 6 years old when it died, was calculated by him and Dean to have been more like 3 years old at death. The two researchers later that year published data on nine early hominids of various species, including early *Homo*, reporting that prolonged infancy had apparently not yet evolved in these animals. "These results reflect a dramatic advance in our appreciation of the biology of these species which have, until now, been regarded in 'human' years," they observed. The first blow had been struck.

There are in fact two major areas of difference between apes and humans in the development of their dentitions during infancy. One is in the pattern of eruption of teeth. For instance, in apes the canine teeth emerge later in relation to the first molars than they do in humans. The second is the time over which tooth eruption takes place. The three molar teeth in apes appear at ages 3.3, 6.6, and 10.5 years. By comparison, the ages in humans are 6, 12, and 18 years. "The reason that human dental maturation is prolonged," observes Lawrence Martin, an anthropologist at the State University of New York at Stony Brook, "is because there is a pause between the formation of each individual molar crown."

The consequence of this combination of differences in eruption pattern and timing is that if you have a human jaw in which the first molar has just erupted you know that the individual was about 6 years old. If the jaw is that of an ape, however, then the individual would have been about 3 years old. However, when you have a jaw of an early hominid and you are trying to establish what kind of growth trajectory is being followed, you cannot assume it is following one particular time scale or the other. You need some kind of absolute scale, and that is what Bromage and Dean claim to have produced.

The Taung child *was originally thought to be about 6 years old when he died, based on human dental criteria. New approaches indicate the age was more like 3 years.*

Using incisor teeth only, Bromage and Dean estimated the age at death of the individual involved by counting a series of tiny ridges on the surface of the enamel, called perikymata, which they say represent a weekly periodicity. Onto this figure they added an estimated time—6 months—for the period when the perikymata do not become visible on the surface of the tooth, another 3 months for the period between birth and the beginning of incisor crown formation, and then a figure for root formation time, if any has begun.

Using this technique on a fossil jaw from the site of Laetoli in Tanzania, for instance, they came up with an absolute age at death of 3.25 years, which has an impressive ring of precision to it. By comparison, if typical human dental growth characteristics had been used to age the jaw it would have been said to be 4.45 years. Similar discrepancies between absolute ages and "human" year aging were found in fossil hominids from South Africa and Kenya. "This was very impressive," says Martin, "and a lot of people were apparently convinced by it."

Meanwhile Smith was finalizing her reassessment of Mann's eruption pattern work. "The reason I did the study," says Smith, "was to make use of the new dental standards that Alan didn't have available to him." These standards are meant to give figures for the typical human dentition and for the variability around the mean. "Alan had to use old standards, some of which went back to the 1930s," explains Smith. "The old standards and the new ones I was able to use are more unlike each other than either is from apes. That's how bad the old standards are."

The way you judge the tooth eruption pattern in a jaw is to assess the degree of development of each tooth (crown half complete, crown fully complete, and so on), and then assign each an age according to, say, the human standards. If the pattern is indeed human, all the teeth in the jaw will be consistent with each other, and each will therefore give the same age. But if the jaw is an ape's, then, because ape teeth erupt in a different order, the human ages attributed to the teeth will be inconsistent with each other. Hence the need for good standards.

Using what she believes to be the best standards available, Smith applied this test to 20 early hominid fossils from South and East Africa and one, a Neanderthal, from Europe. Her results were surprising. For *Australopithecus afarensis*, which many believe to be the earliest hominid so far discovered, the dental pattern was clearly that of an ape. Also strongly apelike was *Australopithecus africanus*, which is a descendant of *afarensis*. The fact that these two australopithecines apparently have an apelike dental pattern was not too difficult an idea to swallow, because apart from being bipedal they are not strikingly human. But the discovery that *Homo habilis* also fell into this category was more significant. *Homo habilis* lived about 2 million years ago, but already had a markedly expanded brain. Smith's data for *Homo erectus*, the putative descendant of *Homo habilis* and possible forerunner of modern man, were more equivocal, but she guesses that they too do not qualify as human using these criteria. The Neanderthal child does, however, seem to have evolved the modern pattern.

These data would seem to suggest that, contrary to what has been believed for more than a decade, the modern human dental pattern—and the prolonged infancy that seems to go with it—made its appearance relatively recently in the course of human evolution. But for one thing: the more stocky contemporary of *Australopithecus africanus*, which is termed *Australopithecus robustus*, also has a humanlike pattern.

If this assessment is correct, does it mean that *A. robustus*, which most anthropologists would place on a side branch to extinction, nevertheless nurtured its offspring for long periods as modern humans do? "Almost certainly not," says Smith. "I would assume that this pattern is a parallelism and is not evolutionarily related to the pattern in modern man."

In using dental growth characteristics to assess the humanlike status of an early hominid, two sets of information have to be weighed: one is the pattern of tooth eruption, which Smith has been examining; and the second is the time over which this occurs, which is what Bromage and Dean addressed. Only by combining the specific humanlike eruption pattern with the pause between molar eruptions that produces a prolonged maturation does the fully human growth pattern emerge. "It is obviously conceivable that *robustus* could have a sequence of tooth eruptions like that in modern humans and yet have an apelike timing," says Martin. "Yes, the eruption pattern is only half the story," agrees Smith. "For the timing you have to go with what Tim and Chris have, and what they have shows that the complete human pattern came late in evolution."

For Mann, it may be that he was ensnared in one of those tricks of fate, "a strange accident," as Smith says. Remember, Mann did his initial analysis on the hominids from Swartkrans, and these happen principally to be robust australopithecines, which do appear to have a human eruption pattern. Given the climate of opinion of the time, it is easy to see how Mann's conclusion—including the myriad implications of a prolonged infancy—would be readily, but wrongly, accepted as being applicable to *all* early hominids. "Nonsense," is Mann's reply to such a suggestion, and he hopes soon to publish his critique of Smith's and Bromage and Dean's papers to substantiate his viewpoint.

"I am dismayed when authors present evidence that most readers are unable to evaluate properly," says Mann, "and yet the conclusions are immediately accepted because they fit the current fashion." In the case of Bromage and Dean's work he says that "they don't have the vaguest notion of what perikymata are." Moreover, he contends that "the evidence they present to show that perikymata are laid down in a regular, 7-day pattern is simply wrong." Mann is equally critical of Smith. "If you take her technique of looking at eruption times and plotting them in the way she did, you can use it to show that a sizeable number of modern human children are apparently growing up in an apelike manner." Smith's analysis, he states, "is absolutely and totally wrong."

Dean is the first to admit that he does not know what perikymata are. "Having a 7-, 8- or 9-day periodicity like that in enamel formation is a complete mystery," he says. "Nevertheless, the evidence I've seen on perikymata since we published our results makes me confident that we were broadly right." In fact he says that because they were aware that their message was so revolutionary, he and Bromage probably overestimated the calculated age of their early hominid specimens.

The dispute over the significance of perikymata is at least twofold. These tiny ridges on the enamel surface are manifestations of lines—striae of Retzius—that run from the enamel-dentine junction. These lines are separated by cross striations, which most people—but not Alan Mann—accept as daily increments of growth.

This whole puzzle is clearly going to take some time to settle, and when finally it is resolved the simple dichotomies such as "either human* or *ape" will almost certainly have vanished.

The first question, therefore, is how many cross striations normally separate the striae of Retzius? "In humans it varies from six to nine," says Dean. He cites more than 30 species of animal, including monkeys and apes, in which this kind of periodicity appears to apply. Nevertheless, there is at least one example of an orangutan in which the striae are separated regularly by between 14 and 16 cross striations. "Obviously, I'm not very happy about that," he admits.

Martin agrees with Dean that cross striations probably represent daily growth increments, but is cautious about accepting the idea that perikymata routinely represent a periodicity close to 7 days. "There aren't enough data available to be sure about that yet," he says. Martin and a SUNY colleague Fred Grine plan soon to begin a project that would involve cutting some fossil hominid teeth in half and counting the cross striations and striae. "This should help resolve the issue," he says.

Two British researchers, Bernard Wood of the University of Liverpool, and David Beynon of the University of Newcastle, already have information on the relationship between cross striations and striae in modern human and early hominid teeth. "The data we have can be seen as supporting what Bromage and Dean have concluded," says Beynon. But, being a cautious man, he warns that "there is no absolute proof that the periodicity in fossil hominids means the same as it does in modern humans." As always, although experiments can be done to confirm the weekly periodicity of striae in living animals, for fossil species it must necessarily remain an extrapolation.

Support for Bromage and Dean's work among other anthropologists is therefore at best mixed. Martin guesses that in the end they will probably prove to be correct in essence, but is critical of the precision with which they originally presented their calculated ages, namely to two decimal places. He says that it would have been more in keeping with the "soft" nature of their data if they had said that, instead of being 6 years old as had always been supposed, the Taung child was somewhere between 2 and 5 years. "But no one would have listened to that sort of thing."

A resolution of the strong differences of opinion between Mann and Smith over the correct standards to use the and the proper analysis of data will probably have to await another study by another group. Meanwhile, Martin comments that "Holly's standards are as good as you can get at the moment." He says that although Smith began with an assumption that there were two patterns—human and ape—he would expect there to be several variants, within the hominids and within the apes too. "Her assumption was a good starting point."

In fact, Conroy already has evidence of such variants. He and his colleagues have recently been doing CAT scans on some fossil hominid jaws, including the famous Taung child. The first molar in Taung's jaw is virtually fully erupted, which means that by ape standards the second molar formation would already be well under way; in a human the second molar would be less well developed than in an ape, but nevertheless would show some calcification. "From what we can see with the CAT scan, there's nothing there," he says. "It's bizarre. It doesn't look like an ape or a human to us."

This whole puzzle is clearly going to take some time to settle, and when finally it is resolved the simple dichotomies such as "either human *or* ape" will almost certainly have vanished. ■ ROGER LEWIN

ADDITIONAL READING

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