Paul, the Apostle of Jesus Christ, began his missionary travels from Antioch in Syria, which remained the principal base of his apostolic ministry and the starting point of his missionary journeys to the Gentile world. Antioch was a large cosmopolitan city and one of the first centers of Christianity. Starting in Antioch, both Paul and Barnabas were sent by the Holy Spirit as missionaries. Paul's missionary journeys from Antioch successively widened the geographic and theological horizons of the gospel, culminating in Paul's presence in Rome, the center of the Roman Empire.

The first missionary journey took place between AD 46 and AD 48. Paul and Barnabas set sail from Antioch to Seleucia and crossed to the island of Cyprus, where they preached in Salamis and Paphos. They crossed back to Asia Minor and landed at Perga in Pamphylia. They turned inland toward Pisidian Antioch, Iconium, Lystra, and Derbe. This journey saw the initial establishment of the Gentile churches and the beginning of the pattern of preaching first in the synagogue and then turning to the Gentiles when they met with opposition. After returning to the cities of their first journey and strengthening the new believers, Paul and Barnabas returned to Antioch and gave an account of what God had done among the Gentiles.

The second missionary journey took place between AD 49 and AD 52 and again set out from Antioch, this time accompanied by Silas and, later, by Timothy and Luke. The journey took Paul and his companions through Syria and Cilicia to revisit the churches of Asia Minor before crossing to Macedonia in response to the vision of the "man of Macedonia". In Europe, Paul established churches in Philippi, Thessalonica, and Berea and then continued south to Athens and then Corinth, where he stayed for a year and a half, teaching and organizing the church. From Corinth, Paul visited Ephesus and then returned to Antioch to report on his mission into the Greco-Roman world.

Paul's third missionary journey, between AD 53 and AD 57, was devoted to a large extent to consolidation and teaching. Paul left Antioch and again traveled through Galatia and Phrygia before settling for three years in

Ephesus, which developed into a major center for evangelism in the province of Asia. The gospel was spread to adjacent territories, directly by Paul or indirectly through his companions. Paul then left Ephesus after a period of civil unrest and continued his travels through Macedonia and Greece, strengthening the churches and collecting a financial offering for the believers in Jerusalem. Paul then returned through Macedonia and Asia Minor and then made the final leg of his journey to Jerusalem itself, in spite of repeated divine warnings of imminent arrest.

Paul's journey to Rome took place between AD 57 and AD 62 and was not, strictly speaking, a missionary expedition. In various ways, it was the divinely-ordained culmination of Paul's calling to bear witness before the rulers and the nations, to "enlighten all, so that you may bring me as a present to Christ in Rome, also with joy" (Philippians 2:17–18). Arrested in Jerusalem, Paul was transferred to Caesarea Maritima, where he was imprisoned for about two years. He successfully appealed to Caesar as a Roman citizen and was transferred by ship towards Rome, where, after an adventurous voyage that included a shipwreck on the island of Malta, he finally arrived to make his defense before the emperor.

In Rome, under house arrest, Paul continued to preach the kingdom of God, and "all who were in his house believed, the Lord giving testimony to the word with all boldness" (Acts 28: 31), openly teaching "both the Jews and also the Greeks who were there" (Acts 28:30). Paul was in Rome under house arrest for between two and three years. Paul had long before expressed his desire to go to Rome as a missionary in order to preach the gospel of Christ (Romans 1:13). The Roman imperial capital thus became the symbolic culmination of Paul's missionary journeys, not just because it was the center of world power, but because Paul was free to preach the gospel there without hindrance (cf. Romans 15:22–29). Rome represents the end-point, both literally and figuratively, of the geographical and theological expansion of the early Church.

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